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INTRODUCTION TO MEDICAL CYBERNETICS

by V. V. Parin and R. M. Bayevskiy

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INTRODUCTION TO MEDICAL CYBERNETICS

By V. V. Parin and R. M. Bayevskiy

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ANNOTATION

This book gives an account of the basic problems of medical cybernetics. Information theory, automatic control theory, algorithm theory, and other related concepts are presented in a form which can be grasped by physicians. General questions of biocybernetics, cybernetics of cellular and subcellular structures, cybernetics of physiological systems, problems of neurocybernetics, and the peculiarities of "man-machine" systems are considered. The book devotes a great deal of space to the application of cybernetic methods in diagnostics. The cybernetic aspects of medical electronics are examined. Problems of biological control are considered. The main trends in the development of bionics are reviewed.

The book is intended for physicians of various specialties, for biologists, physiologists, engineers and technicians concerned with medical and biological problems, medical students, and for an extensive audience of readers interested in the application of cybernetics in medicine.

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INTRODUCTION TO MEDICAL CYBERNETICS

V. V. Parin and R. M. Bayevskiy

ABSTRACT. Medical cybernetics is a division of applied cybernetics which utilizes the concepts and achievements of cybernetics to deepen medical knowledge, improve the quality of medical service, and increase the effectiveness of the scientific and practical work of physicians. The main object of the application of medical cybernetics is man. Research on animals and other living systems is a task of biological cybernetics, which is the theoretical basis of medical cybernetics. The problem with which medical cybernetics is concerned can be divided into three groups: 1) diagnostic problems; 2) problems related to the automation of patient services and the creation of automatic devices for medical purposes; 3) problems of the application of cybernetics in specific fields of medicine, e.g., surgery, radiology, or psychiatry.

All of these problems are considered in the appropriate chapters. In addition, there are also other problems of medical cybernetics which are covered only in a general theoretical aspect because they are either the subject of special disciplines and have extensive literature devoted to them (the "man-machine" system) or because there is not enough material available to examine them in greater detail (problems of prognosing pathological processes).

As a synthetic discipline, medical cybernetics takes in various divisions of theoretical, engineering, and applied cybernetics. Theoretical problems are considered in Chapters I and II. There is first a discussion of the elements of cybernetics and then a consideration of the concepts of biological cybernetics.

Chapter III is devoted to diagnostic problems. It is the most comprehensive chapter and is validated by actual experience in employing cybernetic methods for processing medical information. Chapter IV considers the aspects of medical electronics, various automatic devices, problems of biological control, and biostimulants. Chapter V gives an account of the progress made in the field of bionics. Although bionics, strictly speaking, is not directly related to cybernetics, it is historically a division of cybernetics, and the fact that it is presented as the concluding section of this monograph on medical cybernetics illustrates the admissibility of transferring from "active contemplation" to the practical realization of theoretical concepts.

INTRODUCTION /5*

Modern science is characterized by two contrasting tendencies: an ever deepening specialization and isolation of individual "narrow" disciplines on the one hand, in which the specific methods and procedures of the discipline are used and which have a definite goal-directed purpose; the other trend is towards the unique integration of scientific knowledge and the origination of new directions in the zones of contact, as it were, of sciences that are far removed from one another. Examples of narrow specialization in medicine include opthalmology or hematology, while biophysics is an example of a new "synthetic" discipline.

The most striking evidence of the tendency to use all the advantages of a broad generalization of subjects that were far removed from each other until recently (e.g., mathematics and physiology, logic and electronics, automation and psychology) is cybernetics.

The origin of cybernetics has involved the collective work of biologists, mathematicians, and physicists. The famous mathematician N. Wiener organized a group of scientists of various specialties in the U.S. in 1936-1937. The group was made up of a physicist, M. Vallarta, two physiologists, A. Rosenblueth and W. McCulloch, and two mathematicians, J. Bigelow and R. Carnan. The discussions held by this group covered problems that were common to physics, physiology, mathematics and engineering. Particular attention was given to analogies between living organisms and machines.

At the same time, a number of similar associations of scientists sprang up in other countries. A commission for remote control and automation was established in the Soviet Union. The well-known biophysicist P. P. Lazarev was a member of the commission. A British mathematician, A. Turing, published an article concerning the general principles of computers. A French physiologist, L. Lapique, organized a group of scientists to discuss problems related to contemporary cybernetics. A widely known computational mathematician, L. Couffignal, was a member of this group. A. N. Kolmogorov, C. Shannon, J. Neumann, and other authors published important works in 1940-1946 which later became the /6 foundation of cybernetics.

A book by N. Wiener, Cybernetics, was published in 1948. This book laid down the formal rules of an independent science for the new discipline [1].

Cybernetics arose from the depths of biology, engineering, and mathematics significantly earlier than it was formed into an independent science. The accumulation of facts which indicate the common bond between control processes in living organisms and machines, which are frequently surrounded by the same mathematical equations, also stimulated attempts at a theoretical generalization of these facts.

The investigations of U.S. mathematicians and engineers during World War II were of much importance to the origin and subsequent development of cybernetics. A characteristic problem that required the consideration of activities

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*Numbers in the margin indicate pagination in the foreign text.

which are common to man and to a technical system was the control and guidance of antiaircraft guns to fire upon high-speed aircraft. The previous systems, where a man performed calculations according to the data obtained from manually controlled detection equipment, were absolutely unsuitable. It was necessary to predict the direction, airspeed, and flight altitude of an aircraft with a high degree of accuracy. The participation of a human being in these operations introduced inaccuracy and delay. The first electronic computers that simulated the human element together with a means of feedback were then employed. As a result of the feedback, the information from the actuators is evaluated by the control element and new insturctions are issued to correct the operation in accordance with the task that the entire system must perform. It is quite obvious that all the elements of such a system have definite analogies in the functional structures of an organism, particularly in its central nervous system. Physiological terms can thus be used to describe the action of technical automatic systems. On the other hand, physiological processes can be described by such technical and physiological terms as information, communication, relay, feedback, actuators, etc. It is possible to have a single theory, based on laws, that covers the fundamental principles of communication and control in technical automata as well as in physiological systems. This general theory would be dominated by engineering, which finds new principles for designing and constructing refined automatic systems by studying the activity of organisms, and by physiology and medicine, which make it possible to arrive at a physically /7
exact approach to the study of life phenomena, to experimentally and physically verify the propositions made concerning the mechanisms of certain physiological reactions, and to "model" a number of processes.

N. Wiener defined cybernetics as "the science of control and communication in the animal and the machine". The term "cybernetics" comes from the Greek word "Kybernētēs", which means steersman. The art of controlling a ship is implied here. Incidentally, the term "cybernetics" was used by the ancient Greek philosopher Plato in the sense of the art of controlling (governing) society, and the 18th-century French scientist Ampère, when he was compiling his classification of the sciences, singled out cybernetics as the science of control. Problems of control occupy an important place in various sciences. Thus, for example, the control of various technical processes is considered by the theory of automatic control (regulation). Physiology studies the control processes in living organisms. Sociology investigates the control processes in society. The common bond between control processes is exhibited by the possibility of describing them with the same mathematical expressions. Mathematical disciplines are the foundation of cybernetics. The quantitative evaluation of any process or system, no matter how simple or complex it may be, characterizes the cybernetic approach to the investigation of the surrounding world.

Cybernetics is concerned with general laws of control, control systems, and systems that are controlled. The word "system" implies a complex of extremely diversified and interrelated elements. The most diverse interrelationships can be called a system. For example, the heart and vessels make up the cardiovascular system, a driver and an automobile form a system also, the solar system is an astronomical system, and a complex DNA molecule is a system which consists of submolecular elements. Each system also may be considered as a subsystem that makes up part of a larger system.

The concept of a system is so important in cybernetics that we shall describe one variation of classifying systems which was drawn up by Stafford Beer [2]. He distinguishes between simple, complex, and very complex systems, which in turn may be deterministic or probabilistic. Deterministic systems have precisely defined interrelationships, so that it is always possible to predict the following states of the system on the basis of its preceding states. Probabilistic systems do not permit such a prediction. The behavior of probabilistic systems can be predicted with only a certain amount of probability; the /8 greater the probability, the better known the mechanisms of the interactions of its elements. Stafford Beer writes: "A sewing-machine is a deterministic system. You turn the handle and the needle goes up and down. A dog in the majority of cases behaves as a probabilistic system. You wave a bone at him and, quite probably, he will come to you, even with a higher degree of probability; the possibility is not excluded, however, that instead of coming to you, he will suddenly run away". It should be noted that almost any system of a biological nature is a probabilistic system. An example of a simple deterministic system is a circuit composed of batteries, two wires, light bulbs, and a switch. The state of the circuit in this instance is determined quite simply by the position of the switch ("on" or "off"). A digital computer is an example of a complex deterministic system.

An example of a complex probabilistic system is a reflex arc and the elements that enable it to function, and a neuromuscular preparation from a frog that reacts to electrical stimulation is a simple probabilistic system. The human brain is an example of a very complex probabilistic system.

Cybernetics is interested in fundamental probabilistic systems, although deterministic systems are frequently utilized as models. The property of developing and changing its state is a characteristic of cybernetic systems. These systems are dynamic.

Academician A. I. Berg defines cybernetics as the science of optimal, goal-directed control of complex dynamic systems [3]. The categories of optimality and goal-direction are extremely essential here. Optimality implies the minimum expenditure of energy, matter, and information. Goal-direction denotes the transfer of a system to one of its predetermined states. The essence of control is the process of receiving, collecting, converting, and transmitting information; therefore, information also is one of the fundamental concepts of cybernetics along with the concept of a system. In the opinion of A. N. Kolmogorov [4], cybernetics is concerned with the study of any kind of system that is able to receive, store, and process information and use it for control and regulation. A similar definition is given by the Polish cybernetician G. Grinewski [5]: "cybernetics is the science of informed, informing, and informational systems".

Thus, cybernetics studies the structure of cybernetic systems as well as the processes that take place in them.

The study of the general rules that are inherent to extremely diverse (with /9 regard to their nature and the specific mechanisms of their activity) systems requires a great deal of abstraction based on a number of mathematical disciplines: probability theory, mathematical statistics, set theory, functional analysis, combinatorial topology, theory of numbers, abstract algebra, etc. Leaning heavily upon mathematical disciplines in its development, cybernetics thereby promoted their development and the origin of new directions in mathematical science. Thus, for example, mathematical logic and the theory of algorithms have gained very much from their contact with cybernetics. Such mathematical disciplines as information theory, theory of games, linear and dynamic programming, theory of automata, and others arose and became independent fields directly as a result of the development of cybernetics.

By uniting many scientific disciplines, cybernetics has become the science concerned with the general rules of control of various systems. The basis of the common bond established by cybernetics is the concept of isomorphism (isos - equal, morphe - form), which denotes similarity of form in the broad sense of the word; thus, a prescription and the medicine prepared in accordance to it, the history of a disease and the treatment of a pathological process in a patient's body, an ear and a microphone, and so forth, can be said to be isomorphic.

All types of feedback (in communications equipment, in a living organism, in a steam engine) are isomorphic with respect to one another, which makes it possible to describe them with the same mathematical expressions.

Various processes are simulated on the basis of isomorphism. An isomorphic model (hydraulic, mechanical, electrical, mathematical) makes it possible to comprehensively study various actual processes. We know of the simulation (scale models) of large hydraulic power plants, for example, when they are in the planning stage. It is particularly important to emphasize the isomorphism of events, processes, operations, and the information that characterizes them.

If two systems are isomorphic with respect to one another, they can be characterized by analogous signals, i.e., isomorphism of information is observed in this case. Information exists within a system and is determined by the organization of the system. The structure of a system already includes a certain amount of information. The presence of controlling and controlled components, connected by communication channels through which diverse information circulates, is common to all cybernetic systems.

This information is processed in certain parts of the system, as a result /10 of which there is exerted a regulating influence that varies one parameter or another of the part being regulated. The variations that occur according to the feedback principle are considered to be the controlling part, which generates new information that is sent in the form of commands to the part being controlled. The entire control process is directed toward the attainment of a certain predetermined state of the system which is the basis of the program of its activity.

The study of living and artificial cybernetic systems from common methodological positions opens up the possibility of a more detailed analysis of the activity of extremely complex systems such as the brain and makes it possible to utilize the data obtained to construct new and more improved cybernetic machines. The simulation of individual elements of a complex system or the entire system on the whole makes it possible to obtain a better understanding of the principles of its functioning.

There are three divisions of cybernetics at the present time:

1) theoretical cybernetics, which studies problems related to the common mathematical description of control processes;

2) engineering cybernetics, which is concerned with the engineering problems involved in creating control systems and other types of information systems.

3) applied cybernetics, which is involved with the problems of applying cybernetic concepts to various areas of human activity, including medicine.

Medical cybernetics, thus, is a division of applied cybernetics which utilizes the concepts and achievements of cybernetics to deepen medical knowledge, improve the quality of medical service, and increase the effectiveness of the scientific and practical work of physicians. The main object of the application of medical cybernetics is man. Research on animals and other living systems is a task of biological cybernetics, which is the theoretical basis of medical cybernetics. The problems with which medical cybernetics is concerned can be divided into three groups:

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The monograph does not use mathematical apparatus as much as possible, and the few mathematical expressions that were necessary are analyzed and explained in detail. The authors' attempt to make the book accessible to an extensive group of medical workers, in addition, in a number of cases led to a simplified explanation of the problems and forced them to omit certain complicated problems which have a profound academic meaning.

It should be noted that prime attention in this monograph is devoted to the most urgent applied problems and they are discussed on a level that can be understood by physicians of various specialties. The bibliography given at the end of each chapter will enable the reader to become acquainted with the primary sources cited in the text.

In distinction from the authors' earlier published book on the same theme[1], the purpose of this monograph is not to provide the reader with a simple acquaintance with the problems of medical cybernetics, but to give a systematized account of its fundamental positions in order to stimulate the more extensive use of cybernetic concepts and methods in medical practice. This monograph, however, does not pretend to give a complete account of the problems of medical cybernetics since the sphere of application of cybernetics in medicine expands with every passing day. /12

The authors thought it feasible to present this monograph to the readers as an introduction to medical cybernetics and they hope that it will arouse their interest toward a deeper and more comprehensive study of this new scientific direction which provides medicine with methods of exact sciences and creates a basis for the further development of health preservation on a new and significantly higher level.

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Information Theory

As the science that considers the general rules of control and communication in living objects and mechanisms, cybernetics does not deal with the energy aspect of the work of various systems, but with the information that characterizes this work. Cybernetics is not interested in the number of watts, horsepower, or ergs required to perform a given operation (transporting cargo on a railroad or driving an automobile). Cybernetics is concerned with the investigation of the commands or signals which prompted a particular given operation.

The concept of information is widely used by cybernetics to study extremely diverse systems and to discover common principles for controlling their work.

Information is a message about the events that take place inside an extremely complex system and its environment. If we consider a complex system such as "man", the information that proceeds to his input is determined by the physical peculiarities of his receiving devices, i.e., receptors. These receiving devices are the eyes, ears, tongue, skin, etc. Although man possess tremendous capabilities in the sense of perceiving extremely diversified information, just as any other system, he perceives only a certain portion of all the external influences that reach him (stimuli). Thus, our visual organs do not perceive light waves in the infrared or ultraviolet region of the spectrum. We have no special organs for perceiving radio frequencies. However, the information about these influences can be picked up by certain devices and converted into a form that is suitable for observation. The process of converting information also is directly related to cybernetics.

The use of information for control purposes, in addition to problems of receiving and processing information, poses problems with regard to its quantitative evaluation.

The quantitative evaluation of information is a concern of information theory, which is essentially the theory of transmitting signals through communication channels. A communication channel as understood in cybernetics is a connection between elements of a system or a connection between the system and an external source of information. The origin and development of information theory was prompted by scientific and technical progress. Processes for transmitting information developed along with human society. Articulate speech as a means of exchanging information promoted an intensification in communications /16 between human beings to a significant extent. Information was transmitted slowly in early times and the process of improving the means for its transmission also was slow. The industrial revolution at the end of the 18th century, which resulted in the extensive use of machines, brought about a sharp increase in the rate of human progress. A sharp increase in communication means began at this time.

The invention of the telegraph (1837) and the radio (1895) made it necessary to conduct research in the area of information transmission. General ideas concerning information are encountered in the works of Leibniz, but works which examined the essence of this concept did not appear until the end of the 20th century. R. Fisher (1921) was the first to link information with probability [1]. L. Szilard (1929) pointed out the possibility of applying the ideas of statistical physics, thermodynamics in particular, to evaluate information processes [2]. The first work to propose a method for the quantitative evaluation of information was written by R. Hartley, *The Transmission of Information* (1928). Hartley formulated the very important proposition that the amount of information is proportional to the number of choices [3]. In 1933, V. A. Kotel'nikov indicated in his work, *The Carrying Capacity of "Ether" and Wire in Electrical Communications*, that a continuous signal could be sent in the form of a series of discrete signals [4]. Kotel'nikov's theorem opened the way to further progress in the creation of methods for the quantitative evaluation of information.

The American scientist Claude Shannon is considered to be the founder of modern information theory. His work, *The Mathematical Theory of Communication*, written in collaboration with W. Weaver, is still considered to be a classic [5]. In this work and others, Shannon formulated the basic propositions of the theory of transmitting information through communication channels.

Figure 1 illustrates the structure of Shannon's general communication system. It consists of five parts.

1. The information source, which selects one of the possible messages to be transmitted.

2. The transmitter, which converts the message in a specific manner and sends out a signal that can be transmitted through the communication channel.

3. The communication channel, i.e., the medium in which the information (signal) is transmitted from the transmitter to the receiver. A noise source is depicted with the communication channel since signal distortions are possible in the process of transmission. Separation of the signal and noise is one of the most important problems of information theory.

4. The receiver converts the received signal and translates it back into /17 the original message.

5. The recipient of the information (a person or a device) for which the message is intended.

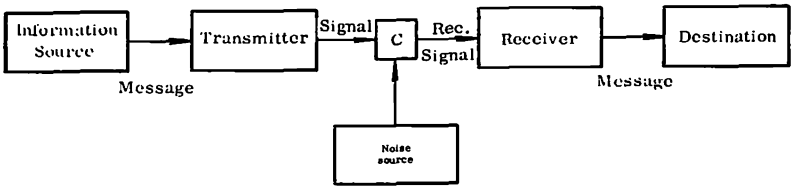


Figure 1. Structure of Shannon's General Communication System.

Let us examine a simple communication channel: book -- eyes -- nerve tracts -- subcortical visual centers -- cerebral cortex. The text contained in the book in this instance is the information to be transmitted. The eyes are the sensors which convert the information into signals that can be transmitted along the nerve tracts. The subcortical visual centers are receivers in this case. They convert the signal until the message is restored. The cerebral cortex is the recipient of the information. If additional visual stimuli occur during reading (e.g., a bright light is flickering nearby or the illumination of the book pages changes) interferences (noise) will develop, which will make it difficult to restore the message. It would be difficult to read the text under conditions of poor lighting.

The message source can be a book or a person, or any biological object. Each message source is characterized by a large number of possible states which are known as symbols, and the total set of symbols that are possible for a given source is called the alphabet of the message. Thus, the alphabet of messages in the telegraph transmission of a text consists of 32 letters, 10 numbers, 10 punctuation marks, and about 12 service signs, i.e., a total of 64 symbols. When a physician auscultates a patient, he deals with information in the form of acoustical phenomena whose symbols are characterized by spectrum, timbre and amplitude. The image of a patient's heart on an x-ray screen also is a message whose alphabet is composed of symbols, i.e., the elements of the image which have a different brightness. Signals are the information carriers. They can exist in various forms: e.g., in the form of electrical signals, pneumatic signals, acoustical signals, etc. Each signal can carry information only within the confines of a specific system. Thus, a human being does not perceive signals /18
in the form of electromagnetic waves of the radio spectrum. Conversely, a radio receiver does not pick up the acoustical signals of human speech. The conversion of one signal into another that is more acceptable for transmission through a given channel is known as encoding. Problems of optimum encoding occupy a central position in information theory [6], but before discussing them, we shall become acquainted with the methods of estimating the quantity of information.

The basis of the concept of information is the proposition concerning the possibility of the occurrence of any event. When we read a new book, we do not know its contents in advance; consequently, we will obtain specific information on each new line and page. If we have already read the book, we would not obtain any new information.

Let us assume that we are watching a football game. The situation on the field is in a definite state, one of numerous possible states, at every given moment. If a certain signal corresponds to each possible state, the transmission of any specific signal will be characterized, on the one hand, by the position of the teams participating in the game at the given moment and, on the other hand, it will simply denote the selection of a specific signal from a set of possible ones. These signals, however, can be used not only to transmit messages concerning a football game, but also to describe other events: e.g., a stage of an industrial process, the results of a physiological experiment, the condition of a patient, etc. (i.e., regardless of the specific sense of the message being transmitted).

It is necessary to digress from the content of the signals for a quantitative evaluation of information. The signals must be considered abstractly. Cybernetics considers information outside of the relationship to the nature of its source. Material information carriers can be light, sound, letters, numbers, magnetic tape, chemicals, etc. But the laws of transmitting, receiving, and processing information are the same for all types of cybernetic systems. It is precisely this condition that gives cybernetics the character of a synthetic science.

The quantitative evaluation of information is closely related to the concepts of the theory of probability. Since the transmission of information denotes the selection of one signal from a set of possible signals, an extremely important value is taken on by the probability of choosing a given signal. It is necessary to consider the number of signals from which the choice is made, /19
as well as the character of the choice itself. The most elementary choice is that from two equiprobable possible states of the "yes" or "no" type. For example: it is necessary to choose one book from two new ones. There is uncertainty before the choice is made, and the uncertainty is eliminated after the book is selected. A similar choice from two equiprobable states is quantitatively evaluated as one binary unit of information.

All messages can be reduced to a binary message; since each binary message contains one binary unit of information, the number of binary units in any message can be determined by the number of binary questions that it contains. A binary question requires only one of two possible answers: "yes" or "no".

But each question can be given a statistical answer in addition to the categorical "yes" or "no" answer. For example, the question "will it rain tomorrow" can be answered by "no" or "the chances are 10 out of 100 that it will rain" or "yes" or "the chances are 90 out of 100 that it will rain". These pairs of answers are practically equivalent, but the statistical answer is more correct since it considers the probability of one event or another. The categorical answer contains more information than the statistical answer since the latter has uncertainty. There is more uncertainty in the answer "the chances are 10 out of 100" than in the answer "the chances are 90 out 100".

Thus, the statistical answer contains as much information as the categorical answer minus the uncertainty. The greater the probability of a given event, the smaller the uncertainty. If we say that the probability is equal to 0.99 (i.e., 99 out of 100), the uncertainty would amount to only 1% ($1.0 - 0.99 = 0.01$). If the probability is equal to one, there is no uncertainty. The obtainment of a message denotes the elimination of uncertainty: the greater the uncertainty was, the more information obtained as a result of its elimination. Indeed, if a good therapeutic effect from some medicine is rated with a probability of 0.2 in one case and 0.9 in another case, then, after receiving the message that the patient became better as a result of taking this medicine, we would obtain significantly more information in the first case than in the second.

For two equiprobable events (their probabilities are equal to 0.5 and 0.5) a single choice denotes that the probability of one event will become equal to 1 and the second event will be 0. One binary unit of information is obtained in this case. Two successive choices are made for four equiprobable events. For example, we have four boxes of matches, three of which are empty, and we must find the one that is full. First we choose one pair of boxes (the first /20 binary unit of information) and then we choose the necessary box in this pair (the second binary unit of information). If there are eight equiprobable events, we must correspondingly make three successive choices.

Thus, the quantity of information in equiprobable events is equal to the number of necessary binary choices or the binary logarithm of the number of events:

$$H = \log_2 N,$$

where H is the quantity of information in binary digits; N is the number of possible equiprobable states.

A more complex formula is used for nonequiprobable conditions. It considers the sum of the probabilities of all events. Instead of the number of events in this case, their probabilities are taken into account. The formula for calculating the quantity of information in this case is written in the following way (C. Shannon's formula):

$$H = -\sum_{i=1}^{i=n} Pi \log_2 Pi,$$

where Σ is the summation sign and Pi are the probabilities of all considered events from 1 to n. The minus sign (—) is used because the logarithms of numbers from 0 to 1 are always negative, and the addition of the minus sign (—) transforms the right-hand side of the formula into a positive number; H simultaneously denotes the quantity of information and entropy. The term "entropy" is taken from thermodynamics and denotes a measure of disorder, a degree of chaos. Thus, information may be defined as a measure of order. The unit of measurement of information (or entropy) is the bit (abbreviation of the English expression "binary digit"). The term "binary unit" is often used instead of "bit". The greater the amount of uncertainty eliminated when a message is obtained, the greater the amount of information obtained. The quantity of information can be calculated with the formula indicated above if the probabilities of the occurrence of the individual events are known. For example, a playing die that is inscribed with numbers from 1 to 6 will provide 2.584 bits of information in one throw ($H = - \log_2 N = \log 6 = 2.584$). If four sides of this die are inscribed with 1's and two sides with 2's, the quantity of information is equal to 0.91 bits ($H = - \Sigma\, Pi \log_2$; $Pi = - 4/6 \log 4/6 - 2/6 \log 2/6 = - 0.66 \log 0.66 - 0.33 \log 0.33 = - 0.39 - 0.52 = 0.91$).

As can be seen, when the uncertainty of the outcome is high, the amount of information is greater. When we determine the quantity of information, or entropy, of individual events, we are estimating the value of only one element of the message. An estimation of the entropy of a message on the whole requires /21 a consideration of the number of events that occur per unit time. As applied to a communication system, we can speak of the entropy of the message source (the capacity of the message source). The alphabet of the message in this case (the number of symbols or possible states) and the number of variations, computations, or signals per unit time must be taken into account. This is done by multiplying the entropy of one event (symbol) by the number of symbols per second. Thus, if the results of dice throwing ($-\Sigma$ Pi log Pi = 0.91 bits) at a rate of three events per second are transmitted through a channel, the entropy of the message source is equal to 0.91 x 3 = 2.73 bits/sec (H = nΣ Pi log Pi). The transmission of messages, as we have indicated, requires the adaptation of a signal for transmission through a given channel, i.e., the signal must be translated into an appropriate physical alphabet. Thus, a microphone converts sound vibrations into electrical signals and thereby adapts them for transmission over an electrical communications channel. The recording of an electrocardiogram in the form of a curve on paper or photographic film is also the encoding of cardiac biopotentials into a physical alphabet that we can perceive. Some messages are repeatedly recoded during transmission from one physical alphabet into another before being sent to the recipient of the information. Thus, the mechanical movements of the body in ballistocardiography are converted into relative motions of a magnet and coil, then into electrical signals, then into motions of the recording stylus and, finally, into a visible image, i.e., the ballistocardiographic curve. This type of encoding is said to be nonstatistical since it does not consider the probability properties of the signal. They are the processes of modulation and conversion. If we tried to compose a conditional code, whereby simple symbols (e.g., the digits 0 and 1) would denote the most frequently encountered events, and two-value designations would be assigned to the less frequently encountered events and, finally, three-value code groups would be used to denote events with a very low probability, the rate of transmitting the message would be significantly increased. This is the statistical method of encoding. Maximum redundancy of the messages is eliminated in statistical encoding.

Many of the messages that we deal with in our daily lives and in medical practice possess an expressed redundancy.

For example, one transmission of data on a patient may give the complete history of illness, while another might include only those portions of the patient's history which describe specific complaints, symptoms, or examination findings which have a direct bearing on the further treatment of the patient. /22 Finally, there may be a third case in which a definite code is established, whereby a definite digit corresponds to each symptom, complaint, or examination finding. It is clear that the last method would ensure the fastest data transmission since a maximum amount of redundant signals is eliminated. Redundancy, however, frequently has a definite advantage since it makes it possible to easily correct the distortions that may occur when transmitting signals over a communication channel. Thus, if we designate the words "tachycardia" and "dyspepsia" by the digits 18 and 19, the distortion of one signal (one letter) when transmitting the entire word "tachycardia" would result in a misunderstanding of the word, and more so with regard to the word "dyspepsia". This possibility is not eliminated when these messages are transmitted by a digital code. Therefore, one of the most urgent problems of encoding information is the development of special noise-proof codes. Binary codes, which consider the probability of the signals, belong to this category.

Distortions of a message in the process of its transmission are caused by interferences that may occur in the communication channel, as well as by incorrect selection of the transmission rate. On the one hand, a high transmission rate may cause mutual interference of the signals due to variations brought about by the energy build-up (signal delays) in the reactive elements of the communication line. On the other hand, a low transmission rate (fewer choices per unit time) makes the information at the channel output disagree with the information at the channel input; it is difficult to restore the original information due to the distortion of certain signals. In these cases it is said that the entropy of the message has increased, i.e., its "uncertainty" has increased. The maximum rate of transmission depends on the capacity (C) of the channel, which determines the number of binary units per second. Undistorted transmission of information over a channel requires that the information source be in agreement with the channel characteristics.

As an example, we shall try to determine the capacity of a communication channel necessary for undistorted transmission of an electrocardiogram. If we assume that the optimum amplitude ratios of the electrocardiogram elements are equal to 1:8 (for the P and R waves), and the discrimination of the P wave requires a minimum of two readings, it turns out that the number of possible signal levels is equal to 16, i.e., the possibility of the appearance of any of 16 signals at the channel input is equiprobable.

A determination of the number of readings per second requires a knowledge /23 of the minimum duration of the electrocardiogram elements. If the minimum QRS length is 0.05 sec and the number of readings necessary for indicating QRS is 5 (1 selection every 0.01 sec), the transmission rate (n) will be equal to 100. We shall find the quantity of information contained in the electrocardiogram with the following formula: $N = 100 \times \log_2 16$. It is equal to 400 bits/sec.

Problems related to the transmission of biological information over communication channels play an important role in biological telemetry, automatic processing of physiological data, the creation of various cybernetic models, in the solution of problems of biological control, and so forth.

Information theory presently considers not only channels for transmitting messages, but also channels which symbolize internal communications in organized systems. The stronger the interrelationship between two parts of a system in this case, the greater the amount of information carried by one part with respect to the other [7], and the greater the amount of information transmitted over the channel. Thus, the circulatory apparatus and the external respiratory apparatus form an organized system with an extremely close relationship. We know that the condition of the respiratory apparatus can be judged by a number of circulatory indices. Thus, the respiratory variations of the electrical axis of the heart, the length of the cardiac cycle, and the amount of arterial pressure can serve as a source of information on the rate and depth of respiration upon proper analysis. A smaller degree of communication is characterized, for example, by the kidneys--visual analysor system. From the standpoint of information theory, the investigation of the interrelationship between elements of organized systems consists of finding codes to decipher their messages. The application of information theory to the study of a genetic code and other problems of biological cybernetics will be mentioned later in the text.

In conclusion, we shall discuss the concept of the value of information. As we know, a physician obtains definite information to make a diagnosis when he examines a patient. This information, i.e., its sufficiency for diagnostic purposes, cannot be evaluated in terms of quantity of information. The concept of quantity of information is suitable in this case to investigate the possibility of storing or transmitting the data collected by the physician without scrutinizing it. Estimation of the value of information, its qualitative aspect, requires a semantic analysis. Attempts at such an analysis are contained in the semantic theory of information [8], but the subjective approach to evaluating information on the basis of the level of knowledge of the evaluator is an essential shortcoming of this theory. The recently completed works of the prominent Soviet scientist, Academician A. A. Kharkevich, are of much interest in /24 this regard. Kharkevich [9] has proposed the introduction of a characteristic of the value of information as an increase in the probability of attaining a goal as a result of obtaining information. The value of information (I) in this approach can be determined in the following way:

$$I = \log_2 P_1 - \log_2 P_0 = \log_2 \frac{P_1}{P_0},$$

where P_0 is the probability of attaining the goal before obtaining information; P_1 is the probability of attaining the goal after obtaining information. The value of the information is measured in bits. The value of the information can be positive or negative, depending upon whether the probability of attaining the goal is increased or decreased after obtaining the information. In the example of the physician who collects information to make a diagnosis, each diagnostic test can be mathematically evaluated and then, by using cybernetic methods, the sequence of the tests can be determined for each given case in order to make a diagnosis in the shortest length of time.

Information theory is the mathematical foundation of cybernetics. By using the same methods for investigating living and nonliving systems, cybernetics promotes the mathematical generalization of a number of biological laws. In connection with this, broad prospectives are opened up to biologists with regard to new advances in theory and practice in the fields of medicine and physiology. As Karl Marx once said, "science will achieve perfection only when it succeeds in using mathematics". The use of cybernetic concepts in this case, and information theory in particular, will promote the further improvement of biological science.

Feedback

One of the fundamental principles of all cybernetic systems is the feedback principle. Feedback is the return flow of information in a control system, i.e., the obtainment of information by the controlling element on the element being controlled. The information obtained as a result of feedback is used to correct the control process and to make the necessary changes in the state of the element being controlled. Thus, any control system can be characterized by the following three conditions:

a) direct communication between the controlling and the controlled part of the system, through which the control signals are sent; /25

b) feedback between the controlled and controlling parts;

c) processing of information on the current status of the control system through the feedback channel into control commands.

A block diagram of a control system with and without feedback is illustrated in Figure 2.

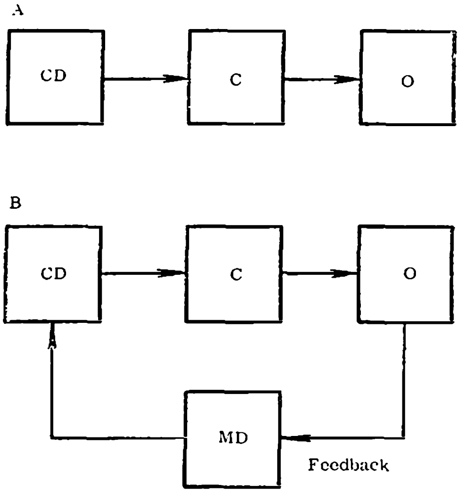


Figure 2. Block Diagram of Control System with (B) and without (A) Feedback. CD = Control Device; C = Controller; O = Control Object; MD = Measuring Device.

Control is accomplished without performance monitoring in systems without feedback. The commands are sent continuously to the actuator according to a specific program. The control of automatic machine tools with programs on punched cards or magnetic tape is set up in a similar manner. In living organisms, as a rule, all processes occur on the basis of feedback. Feedback is of tremendous importance for maintaining constant conditions in organizations (heat regulation, water-salt exchange, arterial pressure, etc.) as well as in the reflex acts and voluntary activity of humans.

The presence of a measuring device, which makes it possible to monitor the status of the actuator and make decisions in accordance with the information obtained, radically changes the behavior of a system, makes it more flexible, and less subject to disturbing and damaging external influences. A detailed analysis of the value of the feedback principle in physiology will be given in subsequent chapters. It is important to note here that this principle is common to all cybernetic systems since the constant active adaptation to changes in the conditions of its activity distinguishes cybernetic systems from other systems. /26

There are two types of feedback: negative and positive. In negative feedback, commands are sent to the controlled object from the controlling device in order to eliminate disagreement between the system's actions and the assigned program. For example, an increase in body temperature in a living organism will lead to expansion of the cutaneous capillaries, which will promote an increase in cooling; an increase of temperature in a thermostat will lead to a decrease in heating and heat generation. The result of the feedback action in both cases is identical, i.e., an abnormal temperature increase is eliminated, but the mechanisms and methods are different.

Positive feedback does not lead to the elimination of disagreement, but to an intensification of it. Positive feedback causes the generation of oscillations in various electronic systems. An example of positive feedback in the human body is an epileptic seizure, when a slight stimulation of a section of the cerebral cortex leads to a sharp increase in the excitability of other sections, which then leads to the excitation of the sensory and motor spheres. It is also possible that several other pathological conditions are based on the mechanism of positive feedback.

Feedback is the basis of self-control in simple and complex systems. The suitable behavior of a system is impossible without feedback, without obtaining information on the degree of proximity to the established goal. The more complex the organization of the system, the greater the role played by feedback in its mutual compensation with the medium and in preserving its internal structure. Simple deterministic systems, generally speaking, do not need feedback. Their reaction is simply determined by strict relationships between the elements and by their purpose. Feedback is the only possible means of existence for probabilistic systems. Disturbances can be compensated for in these systems by using feedback regardless of the nature of the disturbances.

Feedback-based regulation is used by living organisms as a method of adjusting to living conditions. Feedback became the universal means of interaction of biological systems with the surrounding world in the process of evolution. In distinction from a technical system, biological feedback is characterized by nonlinearity, i.e., there is no direct relationship between the output information and the result of correction. Let us consider a simple example. We extend our arm to pick up a pencil from a table. The motion of our arm is constantly monitored by the visual and kinesthetic analysors. The information from these two analysors goes to the brain, where it merges with the goal-achievement program, as a result of which correcting commands are generated. The nearer the hand moves in the direction of the pencil, the greater the effect of the information from the analysors on the activity of the effectors. Finally, the sensitivity of the system to the feedback signals becomes maximum somewhere /27 near the goal, and this ensures the exact coordination of the specified motion. Here is one more example: the reaction of the pupil to light (the greater the light flux, the less sensitive the system for regulating the pupil size).

Feedback is employed most often in engineering with a linear relationship since systems of linear differential equations are well suited to it. Nonlinear relationships require the creation of rather complicated devices to simulate the corresponding relationships betweeen commands and effects. Maximum adaptation is provided by nonlinear feedback in biological systems due to extrapolation of the response. Maximum response of a living organism occurs when the analysors send a maximum signal. This ensures maximum accuracy of regulation and makes it possible for the organism to partially avoid influences that may be extreme.

An explanation of the laws of feedback in an organism and the mathematical description of them will make it possible not only to profoundly understand the essence of physiological (biological) mechanisms, but will also point out ways of influencing these mechanisms, in addition to being useful to engineering (bionics).

One more important feature of biological feedback should be noted: the delay effect. Any action of an organism entails a certain amount of delay (latent period of response). This delay depends on the time of travel of pulses through the nerve tracks, on the time of actuation of hormonal mechanisms, etc. Delay in linear systems is related to the appearance of oscillations, since if /28 the compensating effect is exactly proportional to the disturbance, the continuing action of the disturbing factor will lead to a build-up of errors during the time in which the correcting mechanisms are actuated. A new reaction of a system also occurs with a delay and the reaction again does not correspond to the disturbance at the moment that the correcting command is sent. Thus, oscillations occur in the reactions of the system, and the system is "self-excited". Nonlinearity of feedback and the "exercise effect" are the measures that were evolved to prevent oscillations in systems and to increase their accuracy.

In conclusion, we should mention the interaction of several feedback networks that act in opposite directions, provide an associated reaction to various disturbances, or perform functions of approximate and precise regulation.

A living organism provides numerous examples of this sort of feedback, some of which will be considered in later chapters.

The concept of feedback has an exceptionally important meaning in cybernetics. The behavior of complex feedback-based systems takes on completeness, order, and expediency. Wiener characterizes feedback as "the property that makes it possible to regulate the future behavior of orders which were executed in the past" [10]. The consideration of the differences between an action and its result is the main essence of feedback mechanisms, which are absolutely necessary if we are to concern ourselves with the equilibration of a complex probabilistic system with the dynamic conditions of its medium.

Algorithms

As the science of control processes, cybernetics is concerned with the processing of input information into control signals. A control process, in essence, consists of making a decision on the basis of certain input data. This decision is the command. A precise instruction for a certain system to execute actions or operations in a specific order is called an algorithm. The term "algorithm" is derived from the name of a famous Uzbek [sic] mathematician, Mohammed al-Khwarizmi, who lived in the 9th century and wrote one of the first textbooks on arithmetic, in which a system of strict rules was first established for arithmetical operations with numbers.

Any control process is accomplished according to specific laws and, consequently, has an algorithm. Control is an algorithmic process since it concludes with a decision, i.e., a command. Control processes in a living organism also are accomplished in accordance with specific algorithms. The search for algorithms essentially comprises the content of a number of theoretical biological and medical sciences such as biochemistry, physiology, certain areas of biophysics, ecology, and others. The development of cybernetics made it possible to apply mathematical methods in the investigation of control systems and, in particular, the experience acquired in the area of the theory of algorithms. This theory appeared long before the birth of cybernetics and it has been employed quite extensively in connection with the emergence of electronic computers. Modern electronic computers make it possible to solve practically any problem if an algorithm for its solution is known. In a simple case, the *algorithm* may be given as a formula. For example, the expression ($a^2 + b^2 = c^2$) is the algorithm for calculating the hypotenuse of any triangle with respect to its sides. /29

Two characteristic features of any algorithm should be noted: determinacy and mass character. Determinacy of an algorithm means that any computer (man or machine) can obtain a correct result by using given rules regardless of its ability. This calculation process can be repeated many times by other computers with equal success. The mass character of an algorithm means that the rules can be used to solve a wide variety of similar problems. In other words, the initial data may differ essentially in different problems, but the very essence of the problems, their formulation, and mode of solution are analogous. Let us consider an algorithm for determining disturbances in the rhythm of the heart (e.g., extrasystoles, Figure 3) as an example. A detailed algorithm can be constructed for a comparison of three successive RR intervals. The following instructions are carried out in this case.

Instruction 1: measure two adjacent RR intervals and proceed to the next instruction.

Instruction 2: compare the duration of the measured RR intervals. If they are equal, proceed to instruction 1. If they are not equal, proceed to the next instruction.

Instruction 3: measure the third RR interval (RR_{III}). Proceed to the next instruction.

Instruction 4: compare the RR_I, RR_{II}, and RR_{III} intervals by means of formulas $(RR_I > RR_{II} < RR_{III})$ and $(2RR_I = RR_{II} + RR_{III})$. If these equalities are observed, make the conclusion "ventricular" and proceed to instruction 1. /30 If at least one of the equalities is not observed, proceed to the next instruction.

Instruction 5: make the conclusion "arrhythmia" and proceed to instruction 1.

This variation of an algorithm for indicating extrasystoles is only an example, and details must be worked out before it could be practically realized by an electronic digital computer. In addition, the following conditions should be observed when carrying out this algorithm.

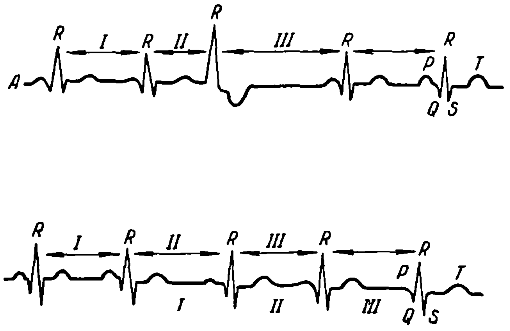


Figure 3. Algorithm for Detecting Extrasystoles (Explained in Text). A = Extrasystole; B = Normal Electrocardiogram.

1. After carrying out instruction 2, the next two intervals should be measured in such a way that the last interval of the first measurement cycle is the first interval of the second measurement cycle, i.e., RR_I and RR_{II} are measured first, then RR_{II} and RR_{III}, RR_{III} and RR_{IV}, and so forth.

2. After carrying out instructions 4 and 5, the next two intervals must be measured, bypassing the three intervals that have already been measured, i.e., begin the measurement with RR_{IV}.

3. The criteria of inequality of intervals must be given in order to carry out instruction 2: for example, calculate if the RR intervals are unequal at 0.85 and 0.87 sec. Obviously, for indicating rhythm disturbances, the intervals would be considered to be unequal if there was a difference, for example, of more than 0.20 sec.

This algorithm indicates that an extrasystolic "diagnosis" can be made by any (human or machine) computer (with the appropriate programming) as a result of formalizing the operations for analyzing the rhythm of the heart. The algo- /31 rithmic description of a biological process makes it possible to simulate the process with electronic circuits or computers, as well as to determine the various parameters of this process according to a certain quantity of known indices (diagnostics). An explanation of an algorithm of the operation of a system requires an understanding of its mechanisms; therefore, the interests of biological cybernetics and physiology are most closely interlaced here, in the theory of algorithms. There is another argument in favor of extensively utilizing the theory of algorithms in biology and medicine. If there are two scientific hypotheses, two methods of making a diagnosis, or two modes of treatment, then, after describing them in the form of an algorithm, it is possible to carefully compare them and select the best one by using mathematical methods and a computer. Algorithms can be very important in designing automatic systems to replace human beings since these systems must be created as models of algorithms of human activity.

We have already become acquainted with two ways of setting up an algorithm: the formula method and the verbal method. These methods are also suitable for the solution of computational problems. But logic problems occupy an essential position in control systems. There are two special methods of algorithm notation for logic operations: the structural method and the operational method. In structural notation, each stage in the solution of the problem is represented in the form of a rectangle in which the content of the operation is notated. Arrows indicate the sequence of the stages. Figure 4A illustrates an algorithm for discerning the R wave of an electrocardiogram in structural notation. The same algorithm is represented in operational notation in Figure 4B. Operational notation entails the use of special signs, i.e., operators. The operators may be arithmetical (A) and logical (P). Arithmetical operators always execute specific commands identically, regardless of the conditions. Logical operators execute alternate commands, depending upon a certain condition. Thus, for example, the logical operator for comparing two RR intervals leads to the execution of different commands, depending upon the result of the comparison. The conditions are usually expressed as $P = 0$ if there is one outcome, and $P = 1$ if the outcome is the opposite. The algorithms illustrated in Figure 4 are examined in detail in the last section of Chapter III.

The algorithms for solving various problems serve as the basis for compiling programs for their solution on a computer. The program is the machine algorithm (see below). The difference between a program and an algorithm consists /32 in the fact that several programs can be compiled to realize the same algorithm. In a biological sense, algorithms may be compared to the mechanisms of various systems, while the program may be thought of as their specific reactions. Reactions can be different, depending upon the conditions. Logical operators that are assigned by an algorithm make it possible to vary the mode of a solution, depending upon one condition or another. Owing to this, every system possesses a large selection of programs that are realized depending upon the circumstances. The greater the number of different programs that can be realized, the more dynamic the system.

Thus, the study of biological and physiological reactions to the action of various factors leads us to an explanation of the individual programs of activity of biological control systems: cell, organ, organism. The task of the investigator is to find an algorithm from a set of programs known to him, i.e., find out the mechanisms of the function. The complexity involved with the study of biological algorithms and programs consists in the fact that even the programs of simple reactions (e.g., the response of an isolated muscle specimen to an electrical stimulus) are formed from a set of sub-programs that belong to cellular and subcellular structures. The transition from one program to another and from one sub-program to another sub-program inside a given program is made on the basis of definite algorithms.

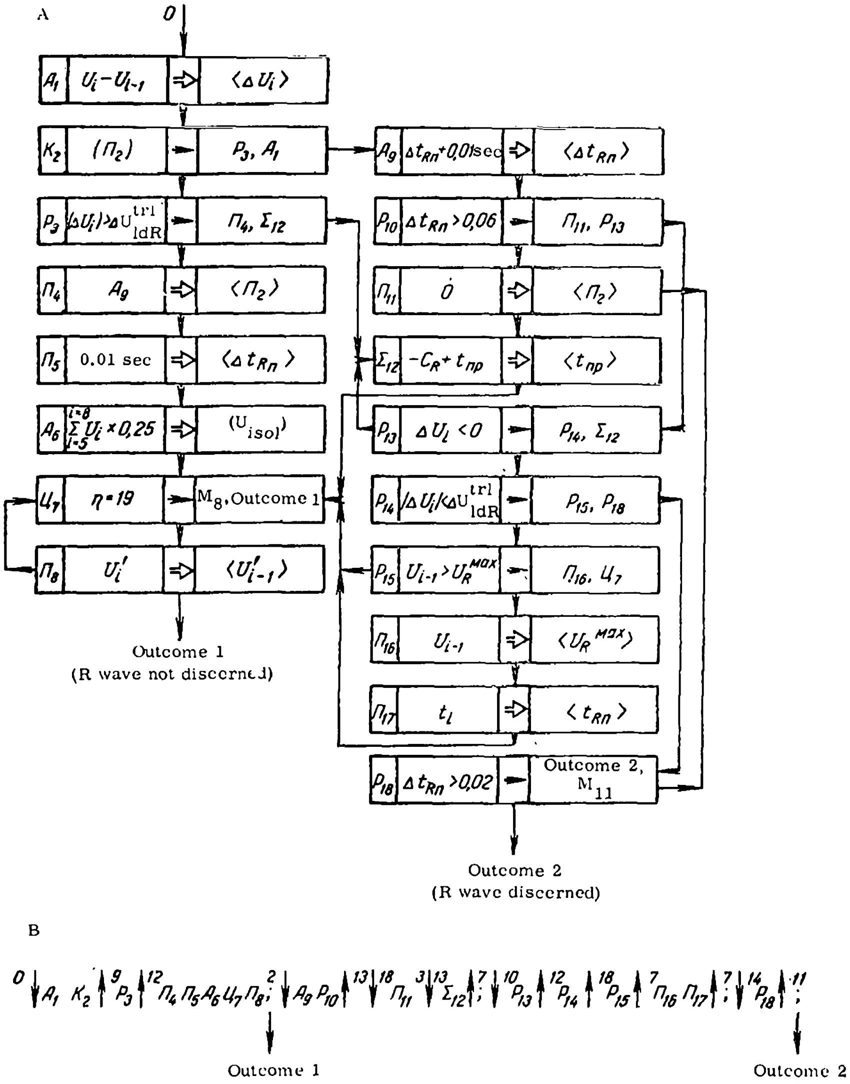

A
0
A_1 $U_i - U_{i-1}$ ⇨ ⟨ΔU_i⟩
K_2 ($П_2$) → P_3, A_1
P_3 $|\Delta U_i| > \Delta U^{trl}_{ldR}$ → $П_4, \Sigma_{12}$
$П_4$ A_9 ⇨ ⟨$П_2$⟩
$П_5$ 0.01 sec ⇨ ⟨Δt_{Rn}⟩
A_6 $\sum_{i=5}^{i=8} U_i \times 0.25$ ⇨ (U_{isol})
U_7 $\eta = 19$ → M_8, Outcome 1
$П_8$ U_i' ⇨ ⟨U'_{i-1}⟩
Outcome 1
(R wave not discerned)
A_9 $\Delta t_{Rn} + 0.01$ sec ⇨ ⟨Δt_{Rn}⟩
P_{10} $\Delta t_{Rn} > 0.06$ → $П_{11}, P_{13}$
$П_{11}$ 0 ⇨ ⟨$П_2$⟩
Σ_{12} $-C_R + t_{np}$ ⇨ ⟨t_{np}⟩
P_{13} $\Delta U_i < 0$ → P_{14}, Σ_{12}
P_{14} $|\Delta U_i| < \Delta U^{trl}_{ldR}$ → P_{15}, P_{18}
P_{15} $U_{i-1} > U_R^{max}$ → $П_{16}, U_7$
$П_{16}$ U_{i-1} ⇨ ⟨U_R^{max}⟩
$П_{17}$ t_i ⇨ ⟨t_{Rn}⟩
P_{18} $\Delta t_{Rn} > 0.02$ → Outcome 2, M_{11}
Outcome 2
(R wave discerned)
B
0 A_1 K_2 9 P_3 12 $П_4 П_5 A_6 U_7 П_8$ 2 $A_9 P_{10}$ 13 18 3 $П_{11}$ 13 Σ_{12} 7 10 P_{13} 12 P_{14} 18 P_{15} 7 $П_{16} П_{17}$ 7 14 P_{18} 11
Outcome 1
Outcome 2

Figure 4. Algorithm for Discerning R wave of Electrocardiogram in Operational (Top) and Structural Notation (Bottom) (According to V. A. Sharov).

Algorithms can be divided into micro-algorithms and macro-algorithms, general algorithms and particular algorithms. This breakdown is especially useful for synthesizing biological control systems, where we encounter a huge complex of phenomena. For the purpose of analyzing the phenomena, the physiologists artificially separate their individual components and perform a so-called "pure" experiment, when all the effects are excluded except the one being investigated. Thus, one of the possible programs of action of a given apparatus is investigated, and one of the features of the micro-algorithm is studied. But a living organism, even on the cellular level, simultaneously realizes a large number of programs and algorithms. The mutual compensation of the organism and the medium or separate elements of the organism is based on dynamic transitions from one algorithm to another, from one program to another. Cybernetics opens up new possibilities to biologists and physiologists in the sense of a synthetic approach to the study of control and information systems of living organisms. Modern computer technology makes it possible to simulate several al- /34 gorithms and programs simultaneously. However, the construction of a model requires a good knowledge of its individual elements. Therefore, the description of data already known to medicine and physiology in the form of specific algorithms is of much interest and value to the further development of biological sciences.

"Black Box"

Cybernetics deals with systems of very great complexity. Such systems, as a rule, do not yield to a detailed description. One of the physiologists' approaches to the investigation of living organisms, as we know, consists of investigating the individual elements of the system, their structure and function, and then attempting to understand the operation of the entire complex on the basis of these elements. This method is called the micro-approach in cybernetics and it consists of studying the algorithms that describe the functioning of individual elements. They are the so-called micro-algorithms. A complex system, a system with a probabilistic organization, has qualitatively new features that cannot be recognized by the traditional micro-approaches of physiology. Cybernetics has worked out its own method, which may be called the macro-approach, but it is better known in cybernetics literature as a "black box" problem.

Let us imagine that we have a box with nontransparent sides, so that the structure of its contents cannot be seen. This box has input and output terminals. An engineer feeds various pulses and voltages to the input terminals and, by observing the signals at the output terminals, he makes a conclusion concerning the contents of the box.

"Black box" problems arise in everyday life, as well as in medical practice. When we receive a letter, we look at the sender's address before opening it and make an assumption concerning the content of the letter on the basis of this look. If we have some information on the sender, we can usually predict the content of the letter with a definite degree of probability. As long as the letter is unopened, it is a "black box". When a patient goes to a physician, an assumption is made concerning a probable diagnosis on the basis of the complaints, anamnesis, examination, and data from a preliminary study. This is also a "black box" problem. When a research worker obtains some experimental /35 data, he works with the data and certain hypotheses and theories, and tries to discover the unknown mechanisms or structures of a "black box". In general terms, the "black box" method consists of making a conclusion concerning the operating principles of a system by observing the inputs and outputs only, and not investigating its structure or the arrangement of its elements.

The "black box" research method consists of studying the information flows and selecting an algorithm that makes it possible to convert the input information in such a way that the state of the outputs is obtained. By performing various tests (experiments) we can obtain some preliminary data that describe the relationships in the "input-output" system. Certain information is required in order to arrive at a conclusion concerning the internal arrangement of the "black box". The greater the number of diverse influences present at the input to the "black box", the less we will find out about the contents of the "black box". In order to establish the interrelationship between the input influences and the output states, it is necessary to perform as many experiments as required to make the variety of their outcomes minimum. If we performed three experiments and have three different outcomes, there is clearly not enough to go on to make a judgement concerning the internal situation in the "black box". If we performed 300 experiments and obtained 10 different outcomes, this would be sufficient for solving a "black box" problem. A variety of "black box" outputs can be handled successfully only with the aid of a variety of inputs. W. R. Ashby called this principle the law of requisite variety. He states it in the following way: "Only variety can destroy variety" [11].

Thus, as a result of a series of experiments, the investigator reduces the variety so much that it is possible to synthesize the system inside the "black box". However, there is a definite limit of information that can be obtained in a "black box" investigation. Ashby considers that a "black box" can be studied with "an accuracy up to isomorphism". In other words, if a mechanism that exactly duplicates the behavior of a black box can be constructed on the basis of the available data, the problem can be considered to be solved. But the creation of an analog of a black box, a device which is isomorphic to it, still does not mean that we have completely figured out the "black box". It is absolutely impossible to test all the conceivable influences and establish all the conceivable relationships between the inputs and outputs. We consciously confine the problem of studying a "black box" within definite limits. For example, we create a control system that performs in a manner similar to a /36 "black box", although the box obviously possesses other capabilities which we have not studied. This is precisely the situation in contemporary bionics (see below), where engineering systems are created that are isomorphic to living systems only in an area of interest to engineers. For example, an electronic computer is isomorphic to certain functions of the brain. When a simple machine corresponds to certain properties of a more complex machine, i.e., when only a single transformation of complex to simple is possible, but not conversely, it is said that these machines are homomorphic. It should be mentioned that in the study of "black boxes", especially if it involves biological systems, their homomorphic representation is possible only in the form of models, actual systems, or algorithms.

It is obvious that the "black box" problem is of importance to the beginning stage in the study of any system and especially in the study of biological systems.

The reflex concept was formed in precisely this way long before the detailed structure of the central nervous system became known. The basis for the creation of this concept was the establishment of the fact that any -- mechanical, chemical, electrical -- stimulation of the skin on a frog's leg, i.e., input of a system, causes a regular reaction at the output -- contraction of the flexor muscles. Subsequent discoveries (establishment of the functions of the anterior and posterior roots, discovery of the sensory, motor, and intermediate neurons, their interrelationships, etc.) essentially only materialized this concept, having described its morphological substrata and the characteristics of the movement of a stimulation in separate parts of the system.

The macroscopic approach by no means should be considered as being primitive and only a beginning research method. In thoughtful regard to experimental results, it often provides sufficiently abundant material for far-reaching conclusions on the functioning of mechanisms hidden from us inside the "black box". It suffices to note that essentially all the fundamentals of the theory of conditioned reflexes were established precisely as a result of experiments that were conducted in this way. Indeed, all the investigations in Pavlov's school employed various combinations of actions at the input of the system -- the receptor apparatus of an animal -- followed by a study of the reactions at the output which occur as a result, i.e., the effector organs and systems -- the salivary glands, muscles, etc. Everyone knows of the large number of deductions that have led to the establishment of very precise regularities of the central nervous system and that these deductions were made on the basis of Pavlov's approach and the methods of his pupils and successors.

Let us mention one more example. A college course in physiology provides /37 us with calculations that make it possible to obtain an accurate idea of the amount of carbohydrates, fats, and proteins that are decomposed in the human body during an experiment on the basis of data on the amount of oxygen, carbon, hydrogen, and nitrogen in the urine or exhaled air. We are dealing only with the beginning element here (the "input") and the final element (the "output"), but we obtain a very far-reaching idea of the functioning of the system.

An approximate knowledge of what takes place inside of one system or another sometimes makes it possible to solve a "black box" problem only on the basis of the "input" data. This was precisely the method employed by D. I. Mendeleyev when he established the composition of a new type of French smokeless powder after being given samples of the cargo that passed through a railroad station in one year en route to a French gunpowder factory.

The "black box" method gives us the key to mastering the possibilities of controlling an enormous variety of complex systems.

As the result of an investigation it is possible to establish a definite number of input conversions, relative to which the output states are invariant. S. Beer considers that a tremendous variety of "black box" states can be reduced

to a number of random search methods, subject to treatment, based on the principle of entropy maximization by means of a dichotomy [12]. This expression, which might seem "odd" to a biologist, means nothing more than a sequential choice from each of two equiprobable states, since maximum uncertainty occurs in this case. For example, we make a choice from two nonequiprobable states ($P_1 = 0.1$ and $P_2 = 0.9$); the entropy is then equal to 0.469 bits ($H = - \Sigma Pi \log_2 Pi = - 0.1 \log_2 0.1 - 0.9 \log_2 0.9$ [sic]. If the probabilities are identical, however, ($p_1 = 0.5$ and $p_2 = 0.5$), the entropy is equal to 1 bit ($H = 0.5 \log_2 0.5 - 0.5 \log_2 0.5 = 1$). As an example of using the dichotomic-choice principle, S. Beer examines the behavior of a system: "automobiles moving in a large city via different routes". The inputs of the system have enormous variety: different speeds, different routes, different driver qualifications, different destinations. Two outputs of the system are considered: 1) the possibility of an automobile collision -- a catastrophe; 2) no catastrophes. It is further pointed out that the entire system is already being controlled by two dichotomic choices. The first choice is the traffic regulation which consists in driving only on the right side of the road (left side = 0, right side /38
= 1). The second choice is a traffic restriction -- traffic lights (0 = stop, 1 = go). These two rules, based on double choices, lead to the fact that the enormous variety of automobiles moving through a large city is transformed into a controllable flow.

The principle of entropy maximization by means of a dichotomy makes it possible to substantially decrease the undesired variety. In living organisms, the observance of this principle results in a goal-directed and advective response to each of the actions instead of a chaotic variety of reactions. A living organism is a "black box" to nature. The variety of its reactions was restricted by means of numerous tests to limits necessary for survival as a result of evolution. In actuality, an organism responds dichotomically to each influence (0 = death, 1 = life). The most complex behavioral acts have been formulated by means of successive dichotomic choices, including mental processes. When we study biological objects, we simulate the influences of nature and try to reduce the variety of outputs of the system being studied. This is done by limiting our interests to a definite group of problems, breaking down a large "black box" into a number of small "black boxes", and attempting to comprehend their contents. The cybernetic approach to the study of complex systems based on the micro-approach introduces essentially new principles into research work and into the practice of controlled actions. We might point out the following problems that are solved in the process of studying a "black box":

-- Determination of the inputs and outputs of the system (the homomorphic approach);

-- Finding the information flows (successive tests for the purpose of limiting the variety of the system's responses);

-- Discovering an information code (finding the necessary dichotomic choices and rules according to which the input states change the outputs);

-- Constructing models that are homomorphic to the "black box" being studied (establishing an algorithm).

In conclusion, it should be noted that the "black box" principle is only one of the possible methods of studying cybernetic systems. We must agree with I. B. Novik, who considers that "absolute reliance on the functional approach of cybernetics which considers objects of the material world as 'covered black boxes' involves the danger of agnosticism" [13]. However, the practical usefulness of this approach makes it an important tool of the biologist and physician, and it is used extensively in the corresponding dialectic sense of knowledge /39 as a process that is developed on the basis of universally historical human practice and founded upon materialistic premises.

The Theory of Automatic Control

The word "cybernetics" is derived from the word "control". The very essence of cybernetics is the study of control processes in machines and living organisms. Cybernetics is called the science of optimal control. "Control" is a very broad concept. In very general terms, control may be defined as keeping a system in order, i.e., arranging it in accordance with a definite objective law in a given medium [13]. Control is the communication process which takes place between the controlled and controlling elements of a cybernetic system. According to V. A. Trapeznikov, control is a correcting action on an object and it involves changing the object's material and energetic resources [14]. In the opinion of A. I. Berg, control is the process of transferring a complex dynamic system from one state to another by means of acting on its variables [15].

A cybernetic system is a combination of a controlled dynamic system and a control system. The general sense of the action of an entire cybernetic system consists in the fact that there is a continual exchange of information between the control system and the controlled system. In addition, external information (influences, disturbances) is sent to both systems. The control system generates the commands, while the controlled system, by altering its states, sends information back to the control system (feedback). New commands are generated with the information obtained from the feedback taken into account. A goal-directed, optimal control process can be accomplished owing to feedback.

Automatic control systems can operate in the following modes: 1) a compensation mode; 2) a servo mode (programmed regulation); 3) a self-regulating mode (self-adjusting systems).

All of these operating modes take place in actual living and artificial cybernetic systems. The deviation-compensation mode consists in the fact that the system constantly eliminates the disagreement between the given state (e.g. temperature level) and the state which develops as a result of one action or another. A deviation from the given state is called the error of the regulation /40 system, and the error itself is the signal (information) which acts upon the controller. An example of a compensation mode of regulation in physiology is the reflex involved in vasodilatation when the arterial pressure is increased, or in miosis when the light intensity is increased. If automatic regulation according to a definite given law (program) is required, the servo mode is used. The system varies its state in accordance with a program in this case.

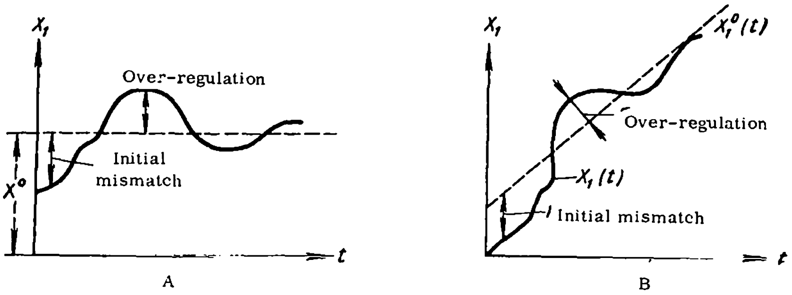


Figure 5. Graphs of a Regulation Process. A = Regulation According to a Given Level; B = Programmed Regulation.

Internal and external conditions may be given as the program in biological systems: e.g., the daily variation of physiological functions (slowing down of the pulse at night, increase in body temperature towards evening, etc.). Machines with programmed control are an example of automatic regulation in a servo mode.

The process of automatic regulation is characterized by variations in the regulated quantity over time. The effectiveness of control depends on the quantitative characteristics of the regulation process and on the parameters of the regulating system. A regulation process can be represented in the form of a graph (Figure 5). The initial mismatch is the difference between the given and actual state of the regulation system. The regulation process is at first related to the inertness of the regulator and to the transitional processes. The faster the state of the regulated object matches up with the given quantity, and the closer the curves of the regulation process are to the given programmed curve, the better the parameters of the regulator. There are stable and unstable systems of automatic regulation [16]. Instability can be related to unaccounted-for influences on the regulated object or incorrect selection of the regulation mode. Instability can be caused by a number of transitional pro- /41
cesses (readjustment, an impulse action).

Problems of the stability of automatic regulation systems are closely related to the biological concept of homeostasis. The term "homeostasis" is derived from the Greek words "homos" (the same) and "statis" (state), and literally means the ability to maintain a stable condition. In cybernetics, homeostasis denotes the process of dynamic balance between a system and its environment. The concepts of homeostasis were developed in biology by the well-known physiologists Claude Bernard and W. Cannon. The term "homeostasis" was suggested by Cannon.

Problems concerned with the balance between living organisms and their environmental conditions have been investigated for some time by various representatives of the biological sciences. I. P. Pavlov devoted a great deal of attention to this problem with regard to the study of the central nervous system [17].

The basic idea of homeostasis consists in the fact that the organism varies its internal and external relationships so as to maintain the constancy of a number of indices of the internal medium which are essential to it. Some biological homeostatic systems will be considered in detail later. We should note here that the concept of homeostasis is closely related to the concept of stability, resistance, and adequacy. The famous cybernetician, W. R. Ashby, worked out the problems of ultraregulation and ultrastability in connection with the behavior of biological systems. He called systems that possess the ability to avoid situations which may lead to their destruction ultrastable systems. Ashby constructed a special device, the "homeostat" (see below), which is a model of an ultrastable system. Ashby considers adaptation as a property of ultrastability. According to his definition, "a form of behavior is adaptive if it maintains the essential variables within physiological limits" [18]. The essential variables, in Ashby's opinion, are those which are closely related to survival and to one another, so that a change in one of them will sooner or later lead to a change in the others. For example, if an animal's pulse rate has dropped to zero, it may be predicted that its body temperature will quickly become equal to the ambient temperature, and that the number of bacteria in its tissues will soon increase from zero (or from almost zero) to a very high quantity. The values of the essential variables are different for different animals.

Adaptation is a version of self-regulation of systems. Self-regulation and self-adaptation are fundamental properties of any large object from a cell all the way to living communities (biocenoses). It is essential that the /42 principles of self-regulation in various living and engineering systems coincide. Feedback mechanisms are the basis of self-adjustment. In 1935, P. K. Anokhin pointed out the important value of feedback, calling it reverse afferentation, for accomplishing adaptive reactions in the nervous system [19].

Before going on to the characteristics of the principles of self-organization of complex systems, we shall consider the main features of biological objects as automatic regulation systems. Any biological system can be represent- /43 ed in the form of a certain structural diagram that includes a control object, controlling element, and feedback. The possibility of a structural analogy between engineering and biological systems (Figure 6) makes it possible to apply methods developed for analyzing and monitoring engineering systems to biological systems. The proportioned-disturbance method can be applied to any system for investigating the quality of regulation. There are various functional tests in medicine which also are proportioned disturbances. Unfortunately, the methods for evaluating the responses to these influences are quite backward as compared to the methods employed in engineering. This has occurred partly because the mechanisms of the reactions have not been studied sufficiently, and the effects of feedback, in particular, have been neglected. In living organisms, just as in engineering systems, there are characteristic transitional processes which bear an individual character and depend on the quality of regulation, i.e., on the adaptation capabilities of the organism. The quantitative

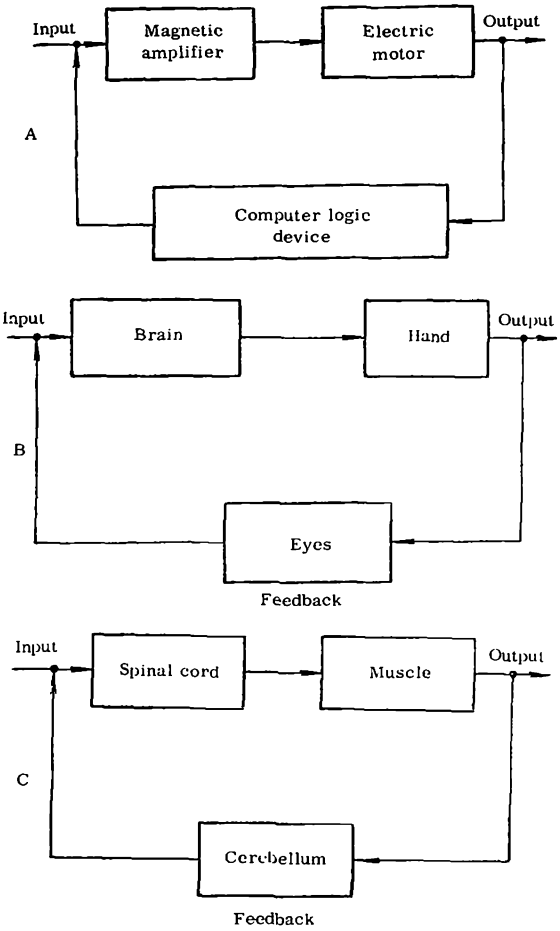


Figure 6. Structural Analogy Between Engineering and Biological Control Systems. A = Engineering Control System; B = Hand Control when Performing a Motor Act; C = Muscle Control when Maintaining Body Equilibrium.

study of the regulation curves in different pathological processes may very well open up new vistas in the diagnosis and treatment of disease.

The peculiarity of living homeostatic systems consists in the fact that regulation is accomplished in them according to the deviation, as well as according to its first and second derivative [20]. Along these lines, some new regularities have been discovered in the reactions of living organisms to certain types of influences: e.g., the law of unidirectional responses (see below). The complexity of the regulatory systems of biological objects is related to their multifaceted character and to a number of self-teaching properties.

"Conventional" control and regulation systems are based on homeostasis and follow specific programs. These systems are elements of more complex cybernetic systems, the main property of which is the capability of self-improvement by means of self-teaching. Purposefulness is of utmost importance in self-teaching systems. The development of living self-teaching systems in the process of evolution was conditioned by the survival instinct in the conflict with unfavorable conditions. Learning is accompanied by an increase in the organizational level of the system, an increase in information and, consequently, a decrease in entropy.

Figure 7 illustrates a block diagram of a self-teaching system. It consists of three blocks: the correcting block, the logic block, and the memory block. The memory block collects data on the situation and stores algorithm alternatives. The logic block works out methods for improving the system in /44
connection with new conditions. The correcting block gives commands to re-adjust the control device in accordance with the results of the logic device [21]. Three methods of operation of self-teaching systems can be indicated.

The first method consists in copying the actions of another, more highly-organized system. For example, a computer duplicates the activity of a research specialist and the environment in which this activity takes place, and introduces corrections into the preliminary algorithm. The second method is based on the random-test method, whereby the system studies how the control has changed as a result of a correction and how much this correction corresponds to a selected criterion. The third method involves a special self-teaching algorithm, whereby the control algorithm is corrected step by step by means of careful consideration of the deviations.

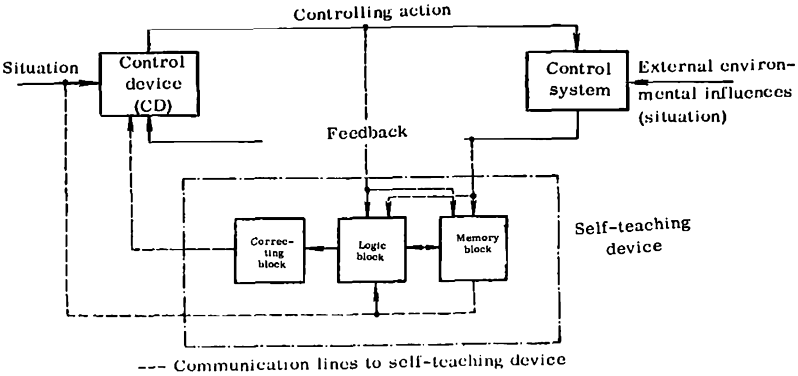


Figure 7. Block Diagram of a Self-Teaching System.

Biological systems are characterized by the fact that their self-improvement is not concerned with any one index, but with an entire system of indices, since many systems of a living organism simultaneously participate in the solution of various problems. Another important property of living organisms is their self-teaching capability based on incomplete information. Instead of deficient information, the system uses the experience it has accumulated and supplements the deficient information with certain general data of a strategic character. S. Beer called this the external complement principle [12]. The complexity of the system is of prime importance for self-teaching. Simple systems are not capable of self-teaching. Statistical systems that take into ac- /45
count the probability of success and systems with negative feedback (e.g., the perceptron) possess the property of learning [22].

The theory of automatic regulation studies simple one-loop systems, as well as multi-loop, highly-organized systems. Along with the deterministic systems which operate according to a strictly defined algorithm, the theory of automatic control considers probabilistic systems that are capable of learning. It is important to note that the existing mathematical methods make it possible to introduce quantitative characteristics of the operational quality of a system without regard to its complexity. This makes it possible to apply the positions of the theory of automatic control in biology and medicine.

Mathematics and Cybernetics

The ultimate goal of the application of cybernetic concepts in biology and medicine is to exert an active influence on living control systems and to maintain their operation on a high level or correct it in a desired direction. Cybernetics considers the living organism as a very complex probabilistic system. A large number of cybernetic concepts help to explain many behavioral traits of living organisms. What distinguishes the cybernetic treatment from analogous positions of physiology, psychology, and other biological disciplines? Some might ask the question: "will medicine learn anything new by considering some reflex mechanism in terms of feedback or information theory?" The answer to these questions lies in the fact that cybernetic terminology is valuable not by itself alone, but in connection with a mathematical foundation which makes it possible to quantitatively evaluate extremely complex phenomena. We know that the empirical approach has been widely developed in medicine. A physician can never predict how a given drug will affect a given patient. To put it another way, he has a general idea of what the effect will be, useful or harmful, but a quantitative analysis of the therapeutic process is not available to him. Another example. A pilot is undergoing a test in a pressure chamber. Physicians carefully monitor his condition so that an emergency "descent" can be made at the very first signs of acute hypoxia. But we cannot calculate individual reactions to hypoxia-inducing effects in order to know the stability limits of a given pilot before the test or right at its beginning. An infinite number of such examples can be cited. /46 But let us now examine an engineer's behavior. A precise calculation precedes the creation of any engineering structure, be it an electrical power plant, automobile, or bridge. The engineer makes specific measurements to detect errors; his "therapeutic measures" are always based on definite quantitative criteria. We are far from asserting the possibility of an analogous approach towards living systems, at least in the near future (however, the rate of scientific development is increasing every year). The introduction of quantitative methods in biology and medicine, however, is a matter of great importance. The further development of life sciences is impossible today without the application of mathematical methods. It is precisely the mathematical approach that will enable us to achieve great advances in the natural sciences.

Cybernetics has possessed mathematical methods since its very conception. Mathematics is the fundamental means of investigating control and communication systems. The cybernetic approach in medicine and biology includes three stages.

1. Manifestation of the analogies between biological and engineering concepts. The formulation of block diagrams of control processes in the living organism. A qualitative description of these diagrams in cybernetic terms.

2. The use of the mathematical methods of cybernetics for a quantitative description of individual elements of living control systems or control processes.

3. Synthesis of the mathematical descriptions of individual control systems and a quantitative evaluation of the organism's reactions.

Biological and medical cybernetics today are concerned mainly with problems in the first stage and shy attempts are being made to enter the second stage. Physicians and biologists already know a great deal about the possibility of a cybernetic explanation of a number of processes in a living organism, but they tend to ignore the possibility of employing mathematics in these explanations. This is why there is sometimes a skeptical attitude exhibited towards cybernetics. However, not everyone realizes that behind every "effective" cybernetic system there lies a possible quantitative approach to analyzing a reaction of a living organism. As we know, medical schools do not teach mathematics. There have been attempts to teach mathematics courses in the biology departments of universities. At the present time, however, there are still no special guides on the application of mathematics in biology, and the existing mathematical guides do not explain how to apply the knowledge obtained therein in biology.

Cybernetics is opening the way for the extensive use of mathematics in the /47 biological and medical sciences. One of the first books to orient physicians and biologists in mathematics was Matematicheskiy apparat kibernetiki [The Mathematical Apparatus of Cybernetics], (1964), by V. I. Chernyshev and A. V. Napalkov. It widely illuminated all the main divisions of modern mathematics and gave good examples of the application of mathematical methods for describing or explaining biological phenomena [23]. We took this book into account when we discussed information theory and the theory of algorithms and, therefore, devoted prime attention to the biological aspect and the treatment of control and communication processes in living organisms from the standpoint of mathematical theories. In this section we shall very briefly attempt to characterize some of the other divisions of mathematics that have been employed in cybernetics and shall refer the reader to the above-mentioned book and other special guides for a more detailed study.

Probability Theory. We have already become acquainted with the concepts of probability (see "Information Theory"). A special mathematical discipline, probability theory, makes it possible to quantitatively evaluate the phenomena that occur in nondeterministic systems, i.e., in those cases when there is no direct correlation between an action and the response to it. The elements of living systems react in precisely this manner; therefore, methods which require a linear and single-valued dependence between the analyzed variables are not very useful for evaluating biological reactions. The concept of the random quantity and random process is the basis of probability theory.

The following are examples of a random quantity:

-- the length of the cardiac cycle

-- the temperature of the forehead

-- an outbreak of influenza in a specific locality

The fluctuations that accompany a regulated process bear a random character. These random deviations may not be considered in exact sciences for constructing models or even for calculations in a number of cases; only the main aspects of the phenomenon may be considered. Random phenomena play an important role in biology when studying a living organism since the number of factors that affect each biological process is very great. Therefore, the application of probability theory, which makes it possible to evaluate processes that have a probabilistic character (i.e., are composed from a set of random phenomena), has an important methodological and theoretical value. The concept of probability and probability distribution as applied to medicine makes it possible to ascribe a quantitative interpretation to many empirical medical criteria. For /48 example, it is known that coronary disease is encountered most frequently in persons over forty years of age, while heart defects are formed most often in individuals under forty. There is almost always a pain syndrome in coronary disease, expressed changes in the electrocardiograms occur quite frequently, and heart murmurs are almost never encountered. Heart murmurs are the most frequent symptom in heart defects, the electrocardiogram variations are usually insignificant (especially in the initial period of the disease), and a pain syndrome is encountered very rarely. Thus, we rate the frequency of diseases and their symptoms with the following words: "frequently", "rarely", "always", "almost never". This is clearly empiricism. Probability theory will make it possible to perform an accurate quantitative analysis in medical concepts of morbidity rate, symptoms, syndromes and indications, and the use of modern computer technology for purposes of diagnostics and scientific research will become possible only after introducing quantitative criteria.

Set theory makes it possible to analyze large sets of objects, their properties, and laws. Since biological systems are very complex probabilistic systems with a large number of constituent elements, the application of set theory to their analysis opens up new possibilities for the quantitative evaluation of biological phenomena. Some examples of sets in biology are the symptoms of a disease, the indications that characterize a specific physiological function, the nerve cells of a nerve center or all the nerve elements that make up the cerebral cortex; and finally, a living organism itself is an example of a set. Set theory makes it possible to solve problems concerning the incorporation of some sets into others (e.g., sets [subsets] of signs which make up different syndromes that are encountered in the same disease). These are problems of differential diagnostics, when it is necessary to decide to which set the manifested symptoms belong or whether two subsets (syndromes) make up the sought set, i.e., disease. Similar problems can be investigated also by determining the sums of properties or products of sets. An important role can be played in research work by methods for calculating the sums and differences of sets. Various functions which have a continuous character can be investigated by the methods of set theory since any continuous curve, according to Kotel'nikov's theorem, can be represented by a number of discrete values. The functional relationships and probabilistic dependences between biological phenomena can be assigned as sets, which then opens the way for their quantitative interpretation.

Queuing theory considers problems related to the servicing of large-scale /49 repetitive processes. The following situation is characteristic for queuing systems: there are several equivalent service channels in which requests for service are made randomly. It is necessary to provide the most optimum distribution of the request flow between channels. The central nervous system, which obtains an enormous information flow and is obliged to form optimum responses, is actually an enormous queuing system. It services the flow of requests from the periphery, from the internal organs, and from the environment, and its work has characteristic features that make it possible to draw an analogy with certain queuing systems. Systems with losses (failures) are distinguished by the fact that if all channels are occupied, a request will leave the system unserviced. For example, if an individual is absorbed in interesting work, he may not hear a call, and two or three repetitions will be required before receiving an answer. Systems with expectation are characterized by the fact that a request which is made at the moment that all channels are busy waits in line for service. An example: an individual may not notice pain when he is in a state of severe emotional excitation; we know of cases when the wounds of mortally wounded soldiers were detected only after the battle. There are pure and composite expectation systems. In pure systems the request must wait until it is serviced. In composite systems the request leaves the system after waiting a certain length of time, and remains unserviced. Many neurodynamic phenomena of the interaction of stimulation and inhibition processes, functioning of the reticular formation, and so forth can obviously be considered advantageously from the standpoint of queuing theory.

It should be borne in mind that the application of this theory, just as the application of all other mathematical theories and cybernetic methods, does not have the purpose of drawing "pretty" descriptive analogies, but is intended for the realistic use of mathematics for analyzing biological laws. For example, the probability of failure (P_{fail}) for a system with losses is determined by the following formula:

$$P_{fail} = \frac{\frac{1}{n}\left(\frac{\lambda}{\mu}\right)^{n}}{\sum\limits_{K=0}^{n} \frac{1}{k}\left(\frac{\lambda}{\mu}\right)^{k}},$$

where n is the number of service channels,
λ is the density of the request flow,
$\mu = \frac{1}{\bar{t}}$ ($\bar{t}$ is the average service time for one request). /50
Σ is the sum of the number of requests that have been made to the system.

This formula may be useful for analyzing the work of a nerve cell, for evaluating an operator's performance in control systems, for calculations of diagnostic systems at large medical establishments, etc.

The theory of games considers so-called "conflict" situations in which the participation of two (or more) opponents is characteristic. Similar situations are encountered in the control systems of a living organism and in its interaction with the environment.

In addition to conflict interactions, there also are interactions when the participants have common goals or the tasks of all elements of the system are common to one another. Conflict situations are encountered in the solution of various biological and physiological problems, in diagnostic work, and in developing automatic devices for medical purposes. The choice of treatment is a typical game situation with conflict relationships between the chosen drug, disease symptoms, living conditions of the patient, and possibilities of obtaining the necessary therapeutic effect. The theory of games considers a set of rules which have their own outcome-probability distribution for each move. The game is a mathematical model of an actual situation. The moves may be personal (an active, conscious choice from alternatives of a series of possible choices) and random (a random choice).

The set of rules that govern a player's choice of moves is called the strategy. Each player can have several (a finite or infinite number) strategies, each of which may lead to a more or less positive result. The result of a game is commonly rated as a numerical function of the player's advantage. This function can be expressed by the probability of gain. A game is said to have a zero sum if one player wins what the other is playing for, i.e., the sum of the gain is equal to zero. For a game with a zero sum, where there are two players (A and B), a matrix can be constructed in the form of the following table (see below).

Each block of the matrix table corresponds to a specific game situation. For example, the average gain for the strategy pair A_1 and B_2 is equal to a_{12}. This means that player A has a definite gain in the given situation which is opposite the gain of player B.

/51

Bj Ai	B_1		B_n
A_1	a_{11}	A_{12}	a_{1n}
A_2	a_{21}	a_{22}	a_{2n}
A_m	a_{m1}	a_{m2}	a_{mn}

One of the important problems of the games theory is the selection of an optimal strategy. The principles of minimax and maximin, the methods of determining the payoff of a game, methods of selecting mixed strategies, etc. [24] make it possible to effectively solve a number of problems of biology and medicine in those cases when they bear a conflict character and can be expressed in terms of the theory of games.

Algebra of logic and binary notation. The interaction of the elements of cybernetic systems, in addition to quantitative relationships, is also characterized by logical relationships. Mathematical logic, a union of mathematics and logic, has been employed extensively in cybernetics. The founder of this discipline is considered to be George Boole, a British scientist who lived in the mid-19th century. Sometimes this branch of mathematics (one of its elements, to be more correct) also is called Boolean algebra or the algebra of logic [24].

Mathematical logic has a system of symbolic notation which makes it possible to write out the fundamental logical operators in the form of formulas. Logical operators are symbols that indicate the relationship between the concepts in a logical process. A total of four logical operators are usually employed in the albegra of logic.

$\rightarrow$ (implies, follows) = implication
$\wedge$ (and) = conjunction
$\vee$ (or) = disjunction
$-$ (not) = negation

Various signs connected by logical operators are united into logic formulas. Each of these formulas is given only two values in the algebra of logic, i.e., it is either true or false, and is frequently designated by 1 and 0.

In connection with the extensive use of the algebra of logic in cybernetic modelling, electronic computer technology, and in the development of various automatic devices, binary notation has taken on significant importance. Binary notation makes it possible to reproduce both quantitative and logical relationships on the basis of relatively simple engineering elements. We have already mentioned the binary questions that can be answered by only a "yes" or a "no". The binary principle is in general use in engineering, everyday life, and in /52 nature. Relays (close - open) and switches (on - off) are constructed on this principle. The binary principle is used when locking a door, putting on overshoes (put them on -- do not put them on), and when purchasing tickets to a movie. A nerve cell can be in one of two states: "stimulated" or "unstimulated".

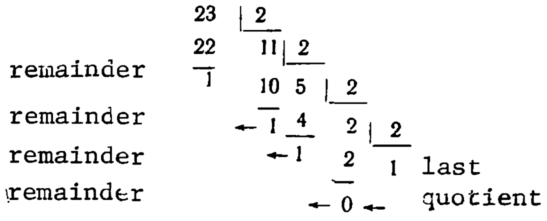
In order to perform calculations and operations with numbers, using only two symbols (1 and 0), it is necessary to change from the universal decimal system to the binary system. Each high-order digit of a number in the binary system is two times greater, not ten times, than the next low-order digit. Thus, the number 2 is represented as 10. After adding 1 to 10 (which denotes 2), we obtain 11 (which will denote 3). The number 4 can be expressed by adding a new digit (11 + 1 = 100). Table 1 lists the numbers from 1 to 20 in binary representation.

TABLE 1.

Decimal numbers	Binary numbers	Decimal numbers	Binary numbers
1	1	11	1,011
2	10	12	1,100
3	11	13	1,101
4	100	14	1,110
5	101	15	1,111
6	110	16	10,000
7	111	17	10,001
8	1,000	18	10,010
9	1,001	19	10,011
10	1,010	20	10,100

To convert a decimal number to a binary number, it must be successively divided by two until a number less than two is obtained in the remainder. A number is expressed in the binary system in the form of remainders, beginning from the end. The last quotient gives the high-order digit of the binary number.

For example:



Direction of Reading Indicated by Arrows.

Consequently, the number 23 will be expressed as 10111 in the binary system. /53

One of the inconveniences of the binary system is the necessity of using a large number of symbols, but this is compensated for by the extreme simplicity of all the arithmetical operations. Addition is governed by the following rule: (0 + 0 = 0; 1 + 0 = 1; 1 + 1 = 10). Multiplication is performed according to the following rule: (0 x 0 = 0; 1 x 0 = 0; 0 x 1 = 0; 1 x 1 = 1). The rules of subtraction and division are just as simple.

The idea of using computing devices to perform logic operations arose with the development of cybernetics. Logic operations can be expressed by the numbers 1 and 0.

If the validity of a statement is designated by 1, its invalidity will be expressed by zero. The operation of negation, thus, can be reduced to substituting a one for a zero or a zero for a one.

A compound premise should be expressed by 1 in performing a logical "AND" operation only if both initial premises are also expressed by 1's. If at least one initial premise is false (i.e., equal to zero), the compound premise also is false (i.e., also equal to zero). It is not difficult to find a complete analogy between the logical "AND" operation (conjunction) and the rules for multiplying binary numbers; therefore, the conjunction is called logical multiplication. The numbers 1 and 0 and the rules for their multiplication can thus be used to perform this operation. The disjunction (the logical "OR" operation) is correspondingly called logical addition. Actually, if at least one out of two premises that are connected by "or" is true, the compound statement is true, and is expressed by the numbers 1 and 0 according to the rules of addition. For example, a patient has influenza or pneumonia. If at least one of these diagnoses is confirmed, the preliminary premise is correct (i.e., 1 + 0 = 1 and 0 + 1 = 1). If, however, neither diagnosis is confirmed, the compound premise is false (0 + 0 = 0). Therefore, the disjunction is called logical addition. The basic logical "not", "and", and "or" operations that we have pointed out can be performed with the aid of various engineering devices.

Figure 8 illustrates block diagrams of logical operations and three types of actual circuits (relay, vacuum-tube, and transistor) for their realization. These circuits are known as the inverter (for performing the logical "not" operation, the coincidence circuit (for performing the "and" operation), and the buffer (it is sometimes called the dividing or collecting circuit), respectively.

Arithmetical operations with numbers also can be performed with the aid of /54 the "not", "and", and "or" logical elements. These logic circuits also are incorporated into the arithmetic devices of contemporary electronic digital computers. Let us consider the circuit of a single-digit adder based on logic elements (Figure 9). This adder has two "and" elements and one "not" and "or" element each. The numbers 1 or 0 are sent to inputs A and B (in the form of electrical pulses: 1 = positive pulse, 0 = negative pulse, or 1 = pulse, 0 = no pulse). Output S is the sum and output C is the carry. Output C is required when the sum is greater than one, i.e., when one more sign (digit) is required for its notation. Thus, the sum of 1 + 1 is equal to 10; the one is carried over to another digit.

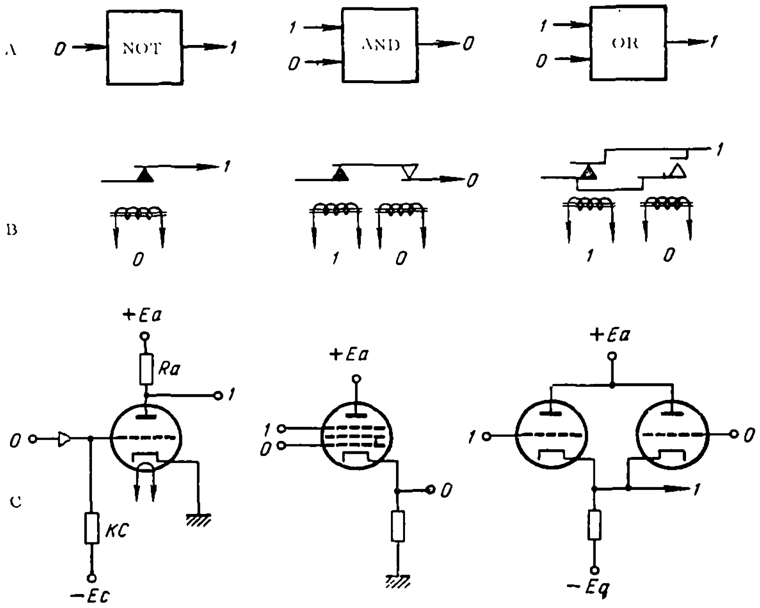
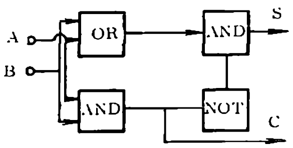


Figure 8. Block Diagrams of Logic Elements (A). Relay (B) and Vacuum-Tube (C) Circuits for Performing Logic Operations.

Logic elements can be used for the technical realization of various logic problems. For example, it is necessary to design a circuit that would switch on an actuating device when a signal appears at two (any) out of three outputs. A similar device may be represented as a simple diagnostic machine which sends /55 out warning signals when a patient's condition becomes worse. The signals are sent out when a combination of two out of three possible symptoms occurs [e.g., tachycardia (A), tachypnea (B), and increase in body temperature (C)]. The logic formula of this problem can be written in the following manner:

P (output signal) $(A \wedge B) \vee (A \wedge C) \vee (B \wedge C)$.



Inputs		Outputs	
A	B	S	C
0	0	0	0
1	0	1	0
0	1	1	0
1	1	0	1

Figure 9. Single-Digit Adder Based on Logic Elements. A, B = Adder Inputs; S = Sum Output; C = Carry-Digit Signal Output.

Figure 10(a) illustrates the functional diagram of a logic device, while Figure 10(b) depicts its schematic.

In conclusion, we shall examine logical operations that are accomplished by diode matrices. A diode matrix is a group of intersecting, electrically insulated, vertical and horizontal buses that are connected across diodes. Input signals are sent to the horizontal buses and output signals are picked up from the vertical buses (Figure 11). A signal appears at the output only when the corresponding vertical bus is not connected to the negative pole of the battery across the switches and diodes. The diode matrix makes it possible to perform complex logical combinations, including disjunctions, conjunctions, and negations/56 Thus, the circuit shown in Figure 11 performs the following logical operations:

$$x = (\bar{A} \vee \bar{C}) \vee D$$
$$y = (\bar{A} \vee C) \wedge (B \vee \bar{B}) \wedge \bar{D}$$
$$z = \bar{D}$$
$$m = A \wedge B \wedge (C \vee D)$$

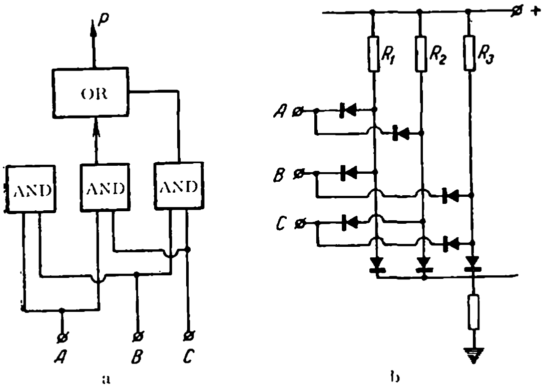


Figure 10. Functional (a) and Schematic (b) Diagrams of Logic Device.

The values of the input signals can signify symptoms and the values of the output signals can denote syndromes or diagnoses. A similar matrix may be considered as a model of a nerve network with several inputs and outputs. A matrix can also be the element of an automatic-control system which makes decisions on the basis of certain logical combinations of biological phenomena: e.g., conditions or indications of selected physiological functions.

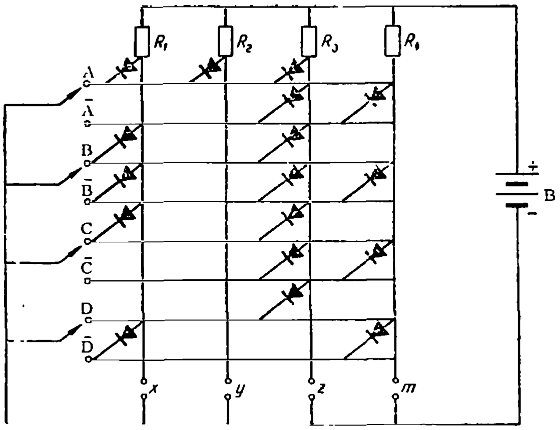


Figure 11. Diode Matrix as a Logic Device.

Electronic Computers

One of the most important practical achievements of cybernetics is the creation of the high-speed electronic computers which have been employed extensively in various fields of science and technology.

The performance of complex calculations, the solution of a number of logic problems, and the storage of information, i.e., functions that were previously considered to be man's prerogative, now can be turned over to a machine. The machine performs all operations a thousand times faster and more accurately than a human being.

There are analog and digital computers. Mathematical quantities are represented /57 in analog computers in the form of continuous values of some physical quantity, e.g., electrical voltage. Analog computers are special-purpose. Each computer is used for the solution of a specific class of problems, i.e., it is governed by one algorithm. Analog-simulation computers have been used quite extensively. They make it possible to solve extremely high-order differential equations, perform integration, and other mathematical operations. There are two types of these computers: problem-solving computers and analog simulators. Problem-solving computers consist of individual units which perform specific mathematical operations. A structural diagram which synthesizes the equation to be solved is created from these units, which are called operational elements. Analog simulators are computers which solve problems by the analogy method. An analog simulator homomorphically represents the object under investigation and makes it possible to study its transformation within the limits of a permissible variety analogy. Analog simulators are used extensively for simulating biological objects (see below). Extremely elementary circuits are employed in this case since the more complex interrelationships in living systems have not yet been studied sufficiently.

In digital computers, numbers are represented in the form of a sequence of zeros and ones (in binary notation). Analog processes are converted into digital processes; therefore, these machines are called digital computers. The main advantages of digital computers over analog computers are high accuracy and universality. The last quality is of particular interest since it makes it possible to solve any problem that has an algorithm for its solution.

Automatic high-speed digital computers are one of the greatest advances in modern science and engineering. Together with atomic energy, the conquest of space, and cybernetics, electronic digital computers have marked man's entry into the second half of the 20th century. It is interesting to note that the main ideas at the basis of the construction of modern electronic digital computers were expressed over one hundred years ago by an English mathematician, Charles Babbage, who worked out the design for an analytical machine. This design had already foreseen the basic elements of modern computers. The principles /58 of contemporary automatic electronic digital computers were formulated in 1946 by the renowned American mathematician, John von Neumann. The first digital computers had very low speeds: the addition of two numbers took up to 0.5 second and division required up to 15 seconds [25].

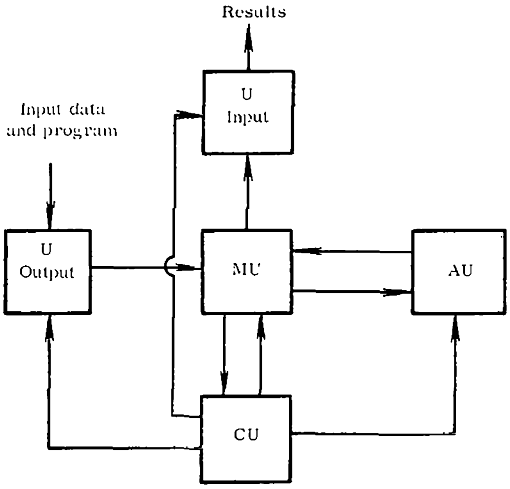


Figure 12. Block Diagram of Electronic Digital Computer.

The first high-speed electronic computer was devised in our country [the USSR] in 1953 under the supervision of Academician S. A. Lebedev. The speed of the electronic digital computers currently being manufactured reaches up to tens of thousands of operations per second, while some experimental models can perform up to a million operations per second.

A general block diagram of an electronic digital computer is illustrated in Figure 12. As can be seen from the diagram, electronic digital computers include the following components:

1) input unit (U input)
2) control unit (CU)
3) arithmetic unit (AU)
4) memory unit (MU)
5) output unit (U output)

The arithmetic unit performs numerical operations. It was indicated earlier that certain logical actions also can be accomplished by means of arithmetical operations with numbers. The numbers that are fed into the arithmetic unit /59 represent the information which the computer obtained from external sources, as well as program data which indicate the sequence of operations. The control unit coordinates the operation of the other units and makes sure that the program is accurately carried out. It gives instructions (in the form of numbers) which control the operation of the computer components that participate in the following operation.

The memory unit functions as an immediate-access storage (it "keeps in mind" the intermediate results of computations) and accomplishes long-term storage of various data required in the process of problem-solving (tabular data, reference material). The computation program is recorded in the memory unit. Memory units are evaluated in terms of the quantity of stored characters (the capacity of the memory unit).

The input unit records the initial data and the conditions of the problem in the memory unit of digital computers. These data are introduced in the form of a definite code, usually binary code, by means of punched cards or punched tapes.

The output unit gives the results of solving a problem. It is usually an alphabetic printer which reproduces the output information from digital computers in a convenient form.

The operation of digital computers is, in general, analogous to how a human being would solve the same problem without comprehending its meaning. After receiving the problem and the instructions for solving it (the algorithm), the individual writes all the necessary data on a piece of paper, which is analogous to feeding the problem and the program into a memory unit.

The sheet of paper plays the part of the memory unit in this case. By performing numerical operations according to the instructions, the human computer sometimes memorizes the intermediate results (immediate-access storage), and sometimes records them (long-term storage). Control of the computation process, i.e., the performance of definite operations at each stage in the solution of the problem, is accomplished by the human computer himself in accordance with the program (information).

The programming of electronic digital computers is a complicated and tedious task, but once the program is formulated an infinite number of similar problems that differ only in their numerical values can be solved. A program is a sequence of instructions given to the machine in order to process the information required for solving a problem. Programming is the technique of writing /60 programs and it is performed by specially trained people known as programmers. The machine language, in which the program is written, is a unique code that has a one-to-one correspondence to definite concepts and definitions of human language. The machine language is most frequently expressed by binary code. It should be noted that almost every machine has its own language, which makes the job of the programmers and the exchange of programs difficult. Much work has been done recently on the development of a universal machine language and methods for translating programs from one machine language into another.

A problem-solving algorithm must be formulated before writing the program. The algorithm makes it possible to automate problem solving. The program is the machine algorithm. The first stage of programming includes the compilation of a detailed diagram of all operations required to solve the problem. The numerical and logical operations, as well as the instructions necessary for controlling the machine, are considered in detail at this time. The second stage consists of compiling the program in machine language.

The input information and program must be fed into digital computers for problem solving. The machine carries out the instructions either in natural order (according to standards) or in compulsory order with an indication of the numbers of cells which contain each subsequent instruction. A cell is an element of the computer memory which is made up of magnetic elements, delay lines, magnetic drums, relays, etc. Each cell position can contain one binary number (0 or 1). The number of positions in the cells of different computers varies from 13-17 to 30-42. Both the numbers and the numerical operations are recorded by means of symbols. For example, 01 signifies addition, 02 denotes subtraction, and 03 indicates division. In order for the machine to perform numerical operations, the instruction must indicate which operation must be executed and with which numbers. The cell which stores the necessary number is called the number address. There can be one-, two-, and three-address instructions. If the instruction indicates the operation code and the address of one of the numbers that participates in the operation, the instruction is one-address. The code of the next operation is taken from the next cell under these circumstances.

A two-address instruction indicates two addresses: the address of the number with which the operation is being performed, and the address of the following instruction. Three-address instructions can indicate three addresses (e.g., the address of two numbers and an instruction address). The following form of a three-address instruction is possible:

02 0111 0471 0643

This instruction is translated in the following manner: "take a number /61
from cell 0111, another number from cell 0471, find their difference (02 is the subtraction code), and record the result in cell 0643".

All numbers are recorded in the cells in binary form: 3 digits are required for recording the number 7 (7 = 111); therefore, seven-digit decimal numbers can be recorded in the 31-bit cell of the M-3 computer since four binary digits (9 = 101) are required for each of the decimal digits (numbers). The long-term memory of the "Ural" and M-3 computers consists of 2048 cells. Instructions or numbers can be recorded in the cells: i.e., the constants required for computations (e.g., the limits of normal values of physiological functions when analyzing the data of a clinical examination). A tentative computer-memory configuration is set up when the program is compiled. This lets the programmer know if there is sufficient space for all the calculation results. Programmers extensively use standard programs for solving separate parts of a problem. Such ready-made subroutines have been worked out for the solution of differential equations, for calculating sines and cosines, extracting square and cube roots, and for logarithmic operations. Programs for interpreting individual physiological parameters (electrocardiograms, electroencephalograms), programs for calculating certain indices (integral power of delta rhythm), and programs for manifesting individual syndromes will be used as subroutines in future diagnostic machines.

The unification of subroutines into new programs is automated, which essentially facilitates programming and makes the programmer's task similar to that of an architect who designs new houses from standard components.

Programming is a long and laborious process in which errors can be made. Each program, as a rule, must be adjusted. The program contains special check signs at each logically completed stage of the program for adjustment purposes. Special test programs or rechecking methods are employed to check the correctness of operations of the computer itself.

In conclusion, we shall trace the process of solving a problem on a computer after the program has been compiled and adjusted. The operator is at the manual-control console (Figure 13). The operator begins the program by pressing the "initial-start" button, after which all calculation-control functions are turned over to the automatic control device and the computer operates until the problem is solved. A set of switches, buttons, and lights is mounted on /62 the console; these elements are used to execute any instruction and to check the status of the computer at any moment of time. After the initial-start button is pushed, a signal is generated which extracts the first instruction of the program from the machine memory and executes it. This takes place in approximately the following way. The memory unit receives the first and second address, finds the indicated cells, and sends their contents to the inputs of all computer units. The arithmetic unit receives the operation code, prepares all the necessary pulses for performing the operation, makes the calculations, and sends the result for notation in the cell whose number is indicated in the third address. A special instruction counter fixes the execution of an instruction and automatically extracts the next instruction from the machine memory. After the computations are completed, the output unit prints the results in octal or decimal notation.

Figure 13. Operator at Computer Console.

Electronic computers are used extensively for solving various nonarithmetical problems and for simulating various algorithms, including the algorithms of biological control systems and diagnostic algorithms. Digital computers have been employed in chess matches, for controlling manufacturing processes, for planning, and so forth.

Simulation /63

Cybernetics widely uses the principles of isomorphism in its study of the functioning of complex systems. When comparing various engineering devices with living organisms, cybernetics considers these devices as simulators of individual aspects of the behavior of animals and man. It is not a question of external identity here, but of the similarity in the functional structure of objects and the unity of the processes of control and communication in living and nonliving systems. Simulation is a new modern method of research that is used extensively in various fields of science and technology. Simulation problems can be developed in different directions in medicine and biology. Thus, a prosthesis for an amputated limb can be designed on the principle of external simulation or on the principle of functional simulation. The last instance is a problem of cybernetics. Simulation of biological objects is based on the analogy between the input and output data of systems that have completely different internal structures. This is actually a "black box" method. An artificial kidney excellently simulates the work of a living kidney with respect to the final effect, i.e., the elimination of nitrogenous waste and excessive electrolytes from the body. This effect is achieved in a natural kidney due to the processes of ultrafiltration, reabsorbtion, and secretion; however, an entirely different mechanism exists in an artificial kidney, i.e., dialysis through semipermeable membranes, the direction and intensity of which is determined by the appropriate selection of the composition of the fluid that surrounds the cellophane tubes inside which the blood circulates.

An electronic analog of a carotid sinus can handle pressure regulation in a specific closed vascular system very well, but, of course, it achieves this goal due to entirely different intermediate and final mechanisms.

When we simulate, we must always clearly define the research problems and must always know exactly which general principles in the operation of the systems being studied are to be reproduced in the given experiment. On the other hand, we must always know which particular aspect of a complex biological process is to be simulated by the given engineering device.

Every model reproduces only some of the aspects of the original, not all of them. Several models, thus, can correspond to one object. The same function can be simulated by different methods: e.g., physical, electrical, mathematical. /64 The electronic and the mathematical methods are the most popular. Physical quantities in electronic simulation are identified with current, voltage, resistance, and other electrical quantities. All conversions of input information are accomplished by means of electronic circuits, while the output information is displayed in a form convenient for perception (printed on paper, depicted on a screen, a graph, etc.). Mathematical simulation is based on the identical expression of phenomena which differ in their physical nature.

The analogy between the mechanical vibrations of the human body that are caused by cardiac activity and the distribution of electrical charges in a circuit made up of an inductance, capacitance, and resistance can be pointed out as an example. Both of these processes are expressed by isomorphic mathematical equations:

$$F = Mx'' + Rx' + Kx \text{ and } E = Lq'' + Rq' + qC.$$

We then have the following analogy:

F = the force applied to the body;
M = the mass of the body;
R = the friction coefficient;
K = the elasticity coefficient;
x', x", x = the displacement, its first and second derivatives;

E = the potential difference applied to the electrical circuit;
L = inductance;
R = resistance;
C = capacitance;
q', q", q = the electrical charge, its first and second derivatives.

The practical use of this analogy has made it possible to create dynamic models of ballistocardiographic systems for investigating the causes of distortion of cardiac forces under various recording conditions. A method was proposed for correcting the distortions in ballistocardiogram recording by the Dock procedure on the basis of a dynamic analogy between mechanical and electrical indices [26].

The creation of mathematical models of various biological processes is an important trend in the development of methods for quantitatively evaluating the phenomena inherent to living organisms.

Simulation in which the problems of studying control and communication in biological systems are of prime importance can be said to be cybernetic. Cybernetic simulation is distinguished by the following features [13].

1. Extensive use of abstract techniques, i.e., "black box" models, widely applied to the most diverse objects, frequently extremely different from one another (e.g., a triode, neuron, and water valve as devices with the same goal-directed behavior). /65

2. The functional approach to models, finding common aspects in functioning, and not in the structure.

3. The study of models as control devices, not from the standpoint of their functional mechanisms.

4. The predominance of mathematical and physical-chemical models with homomorphic representation.

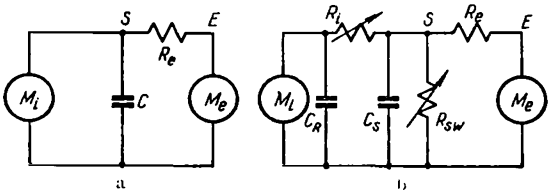


Figure 14. Electrical Model of Heat Distribution in an Organism (see Text for Explanation of Symbols).

5. The extensive use of electronic digital computers for simulation purposes.

Electrical analogs of biological phenomena are the simplest models. More complex models are based on the use of logic elements and a large number of electronic units. They are expressed by more complex mathematical expressions. Finally, electronic digital computers are employed to create models that characterize the activity of an organism's functional systems, the cerebral cortex, or the interaction between a biological object and its environment.

Simulation by means of analogs consists of simplifying the object and reducing it to such a small number of elements that it is possible to obtain a clear idea of its essence [1-27]. Several examples of simple electrical analogs will be given later.

Simulation of heat-exchange processes in the human body [28]. Figure 14,a illustrates a circuit which makes it possible to estimate the temperature distribution and heat propagation in the human body. Current generator M_i functions as the internal source of heat production. Voltage generator M_e denotes the factors that maintain the ambient temperature on a constant level. The heat capacity of the body is replaced by capacitance C, while the heat conduc- /66 tivity between the skin and the environment is denoted by resistance R_e. The potentials at points S and E represent skin temperature and ambient temperature (T_S and T_E), respectively. This model makes it possible to study the time constant of the heat flux with a variable heat load.

$$IRe = T_s - T_e$$
$$T_s = T_s' - (T_s' - T_s^{\circ})e^{-t/ReS},$$

where t is time.

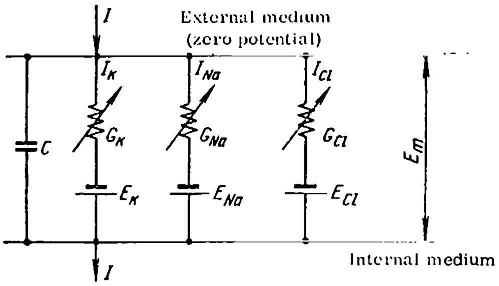


Figure 15. Electrical Model of a Portion of a Nerve Membrane. E_m = Potential Difference Between External and Internal Membrane Surface; I = Ion Flow; E_K, E_{Na}, E_{Cl} = Potential Differences Determined by Difference in Concentration of Potassium, Sodium, and Chlorine Ions; G_K, G_{Na}, G_{Cl} = Membrane Permeability for the Corresponding Ions; C = Membrane Capacitance.

Another analog was developed for a more complete simulation of heat-exchange phenomena (Figure 14,b). C_S and C_R correspond to the heat capacity of the external and internal body layers, $1/R_i$ is the conductivity between the internal and external body layers, and $1/R_{SW}$ is the conductivity determined by perspiration. This analog more accurately represents the phenomena related to heat regulation and adaptation of the body to sharp changes in temperature. The individual elements of the analog can be regulated.

The transmission of substances through cellular membranes. The passive transmission of molecules and ions through membranes depends on the permeability of the membrane and the motive forces. Membrane permeability can be represented as a certain conductivity (resistance). Motive forces can be simulated by an electrical current (battery).

One of the first models of a biological membrane was devised by Hodgkin and Huxley [29]. They consider that the dormancy potential of a membrane is related mainly to a large difference in potassium-ion concentration inside and outside the cell.

Figure 15 illustrates an electrical model of a portion of a nerve. We /67 have conditionally assumed that the potential difference along both sides of the membrane is created by the difference in concentration of the three ions. Although the model is simplified, it has the advantage of providing a simple means of describing currents through a membrane at any potential and makes it possible to easily calculate its variations.

Circulatory system models. A simple model of blood circulation considers only individual aspects of the work of the cardiovascular system. Thus, Bartel's method [30] is based upon the fact that the heart is a pump-valve. The heart valves permit the blood to move only in one direction. The blood flow has a pulsating character. The diagram (Figure 16) represents the heart as a source of pulsed voltage (P), the valves as a rectifier (B), while the peripheral resistance is represented by a capacitor (C) and a resistor (R), which simulate an action and reaction load.

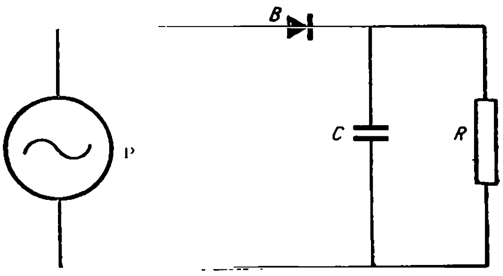


Figure 16. Circulatory Model (Bartel).

Vadot's circuit [31], which consists of 2 resistors and 2 batteries (Figure 17), simulates the interrelationships between the right and left heart and the systemic and pulmonary circulatory systems. An analogous model is shown in the same figure on the right, but the various portions of the blood channel which create a certain resistance to blood movement (the vascular system of the liver, kidneys, etc.) are designated by resistors R_1, R_2, etc.

Ronninger [32] considers the arterial system as a quadripole whose input contains a heart in the form of a voltage source and whose output contains a resistor. (Figure 18). The cardiac output can then be represented as a constant component of the input current. There are other complex models of the circulatory system. Most of them are models of the regulation of various indices. Warner's model [33], for example, makes it possible to investigate the /68 working mechanism of the carotid sinus as a system which is sensitive to the rate of pressure variation (Figure 19).

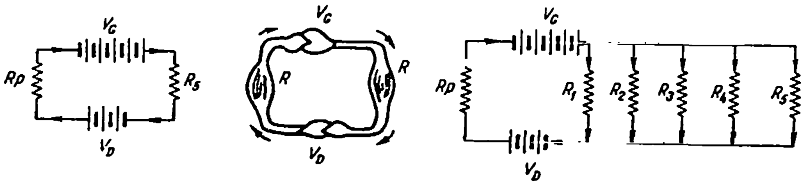


Figure 17. Circulatory Model (Vadot).

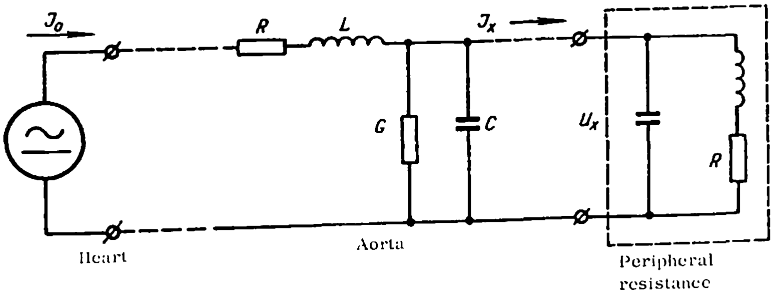


Figure 18. Circulatory Model (Ronniger).

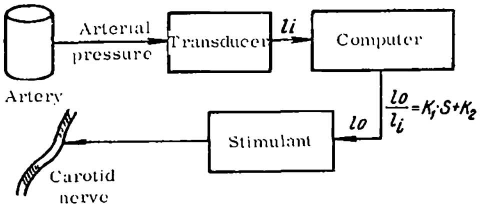


Figure 19. Model of Working Mechanism of Carotid Sinus (Warner).

The transfer function of the carotid sinus has the following form:

$$\frac{n}{P-P_0}=K_1S+K_2,$$

where n is the pulse rate in the carotid sinus; P is the pressure in the carotid artery; P_0 is the minimum stationary pressure at which pulsation can occur; S is the Laplace operator; K_1 and K_2 are constants.

Many models have also been proposed for reproducing the bioelectrical pro- /69 cesses in the myocardium. Among them are the simulators of I. T. Akulinichev, Ye. B. Babskiy, et al. [34], V. I. Zabotin's electronic model [35], a dynamic simulator for research on the effect of body shape on the distribution of cardiac biopotentials [36], etc.

Memory. Memory simulation is a relatively simple engineering problem. The obtainment of large memory volumes comparable to the capacity of the brain is complicated in this case. Various inertial sensors (e.g., heat relays) can be memory analogs.

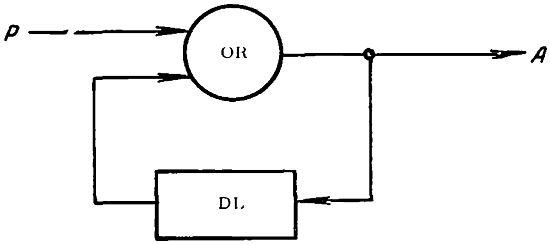


Figure 20. Diagram of Cyclic Memory Element.

A memory cell can be constructed with a capacitor and a resistor. Memory circuits with an unlimited data-storage time are more sophisticated. A simple version of this sort of circuit is a relay circuit with suppression. Ferrite cells and flip-flops are more complicated. A cyclic memory-element circuit (Figure 20) is of interest. The cyclic circuit contains a logic "or" element and a delay line (DL). The pulse to be stored is sent to the input of the "or" element, then from its output A it goes to the delay line, passes through it, and again enters the "or" input. If the delay time is made many times greater than the pulse duration, the circuit can store an entire series of new pulses during the time of its travel through the delay line. Because of this fact, cyclic memory devices can store a significant amount of information [37].

Conditioned reflex. Various electrical circuits and logic circuits of the cyclic-memory type can be used for simulating conditioned reflexes [37]. Let us consider a cyclic circuit for generating a conditioned reflex. This circuit is designed for one coincidence of conditioned and unconditioned signals (Figure 21). /70 A response C is formed at the output of the OR-1 element when an unconditioned stimulus a is introduced. The conditioned signal b cannot go to output C when there is no stimulus a. The signal goes from the output of the AND-1 element across the OR-2 element to the delay line after the first matching of the conditioned and unconditioned stimulus. The pulse is then stored and begins to circulate in the system, periodically going to the AND-2 element.

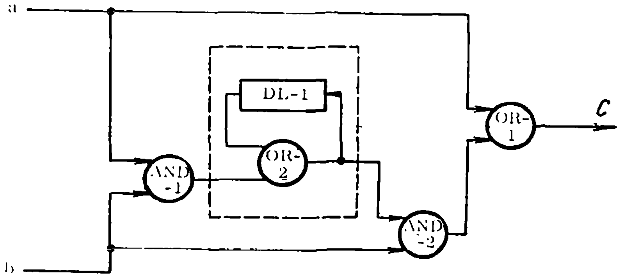


Figure 21. Cyclic Circuit for Generating a Conditioned Reflex (Explanation in Text).

Access to the AND-2 element of the conditioned signal in the absence of an unconditioned signal is now ensured by the passage through the AND-2 element as a result of the matching of the conditioned signal and the signal from the delay line. There are more complicated circuits which simulate the generation of conditioned reflexes after any number of matchings. Experiments with electronic computers are the most convenient means of simulating the conditioned-reflex activity of the brain.

One of the first programs for generating conditioned reflexes (simulation of the learning process) was developed by A. Oettinger [38].

Behavior. The ability of living beings to adapt themselves to their environment is exhibited in the form of behavior related to conditioned-reflex actions. Attempts have been made to simulate "intelligent" behavior of artifical systems. This problem was solved by designing small mechanical devices whose behavior was similar to the behavior of living beings. The first models of "intelligent" cybernetic animals were the "turtles" of the English scientist, G. Walter. They were small wheeled carts with two motors. The "receptors" of /71 the "turtles" were a photocell (the "visual analysor") and contacts which closed upon colliding with an obstacle. An overall view of one of G. Walter's "turtles" is shown in Figure 22. Figure 23 illustrates the electrical circuit of a "turtle". The motors provide forward (M-1) and reverse (M-2) motion of the steering wheel. Each motor can be started (1), stopped (0), or not completely stopped (a lamp is included in the power circuit) by means of relays R-1 and R-2. The motors are started as a result of the activity of the "receptors". Table 2 gives the results of various influences on a "turtle".

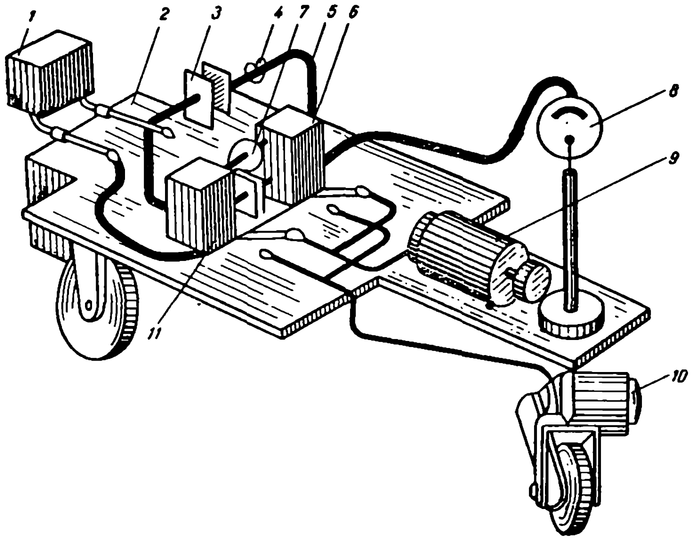


Figure 22. Schematic View of G. Walter's "Turtle".
1 = Power Relay; 2 = Storage Battery; 3 = Capacitor;
4 = Sensory Contact; 5 = Feedback Circuit; 6 = Right
Motor Relay; 7 = Indicating Lamp; 8 = Photocell; 9 =
Steering-Column Motor; 10 = Steering-Wheel Motor;
11 = Second Motor Relay.

TABLE 2. INFLUENCES ON A
"TURTLE" AND ITS BEHAVIOR.

Influence	R-1	R-2	M-1	M-2
Darkness	1	0	1	0.5
Light	1	1	0	1
Blinding	0	1	0.5	1
Contact	0	0	1	0.5

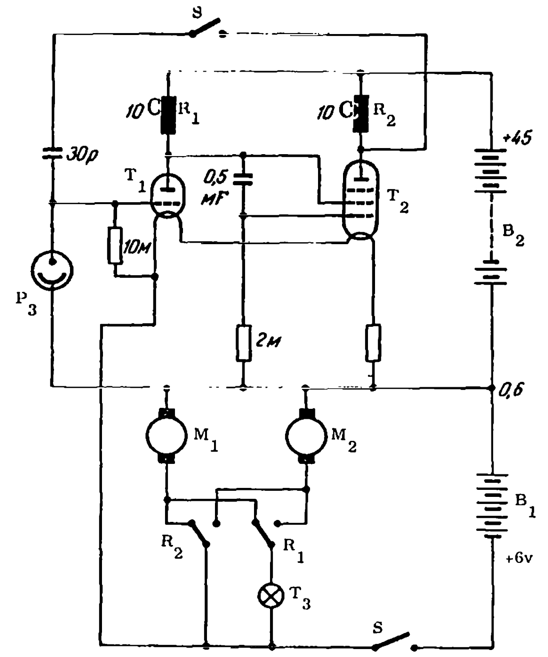


Figure 23. Electrical Schematic of G. Walter's "Turtle". M = Motor; R = Relay; B = Battery; S = Switch; C = "Sensory" Contact.

The condition of the motors is characterized in the following way: 0 = off, 1 = on, and 0.5 = reduced speed.

In all its simplicity, the "turtle's" "behavior" is of definite interest. The "turtle" moves confusedly in darkness. When light appears, the "turtle" quickly "notices" it and moves toward it. When the "turtle" strikes an obstacle, it goes /72 around it. Many variations of "cybernetic animals" and robots have been developed at the present time [37, 39, 41, 42, 43].

The Homeostat. The homeostat of the British scientist, W. Ashby, is a classic device that was developed to demonstrate the principles of ultrastability which characterize a self-organizing system. The homeostat consists of four measuring units, a converter and an analyzing system (Figure 24). Each measuring unit contains /73 a moving magnet which interacts with a magnetic field created by four solenoids. There are needles connected to the moving magnets, each of which can assume one of 25 possible positions. The total number of possible states in the homeostat is almost 400,000 (390,625).

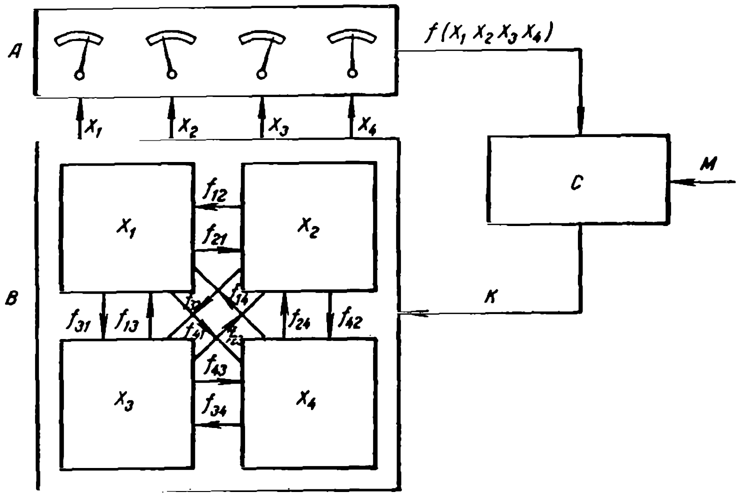


Figure 24. Block Diagram of the Homeostat. A = Indicators; B = Control System; C = Device for Evaluating State of Entire System; M = External Influences; K = Modifying Signals.

After being adjusted to one of these states, the homeostat will return to the given state under any disturbances.

A stable position is found by initially adjusting the units whose coordinates have gone beyond the permissible limits. This principle of adjustment by deviation is being employed more and more in various areas of automation. It is quite probable that homeostat-type devices may be used extensively in a number of engineering systems in the future.

Some other models. The broad possibilities of constructing models on the basis of functional homomorphism have made it possible recently to create a large number of extremely diverse analog and digital simulators. The cybernetic approach to biological and medical problems allows for the use of simulation methods in the most specialized problems. Here is a short list of the biological phenomena and processes whose models have been worked out in one year: /74

-- respiratory-regulation models [44]

-- models of the transport of substances in biological systems [45]

-- a model of sulfate metabolism [46]

-- models for eye-tracking movements [47]

-- pulsation models of the auditory nerve [48]

-- models of epidermal reactions to the action of certain substances [49]

-- models of various clinical situations [50]

-- models of ecological systems [51]

-- models of evolutionary processes [52].

In addition, an enormous amount of literature is devoted to the study of models that characterize the work of the nervous system and the brain [53, 54].

Cybernetic simulation under contemporary conditions is a necessary stage in the development of scientific knowledge [13]. Simulation is the foundation of the cybernetic approach to biological phenomena. The success of the further development of cybernetics depends on this research method to a significant extent.

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CHAPTER TWO. THE LIVING ORGANISM AS A CYBERNETIC SYSTEM

General Problems of Biocybernetics /79

Numerous definitions of cybernetics as a science emphasize the presence of ismorphism between the elements of biological and engineering systems. A living organism on the whole, however, is not the simple sum of the elements which compose it, since the formation of integral biological structures leads to the appearance of new specific laws. The question of the specific nature of biological phenomena occupies a central position in modern science. Neither biophysics nor biochemistry, taken separately, is able to solve problmes of the essence of life. F. Engels wrote: "...An organism is undoubtedly the higher unity which joins mechanics, physics, and chemistry into one whole, since this triad cannot be further divided" [1]. The emergence of cybernetics has made it possible to analyze life phenomena by studying the specific nature of elementary physical processes or other factors which can be described in terms of mechanics, chemistry, or thermodynamics.

Special mechanisms for storing and processing information appear even in the earliest stages of the development of life [2]. These mechanisms are first perfected by means of "blind searching" (trial and error method), then augmented by means of an expedient representation of environmental phenomena; and the complex goal-directed reactions of living systems are subsequently synthesized by means of internal simulation of these phenomena. The concept of expediency generally plays an important role in the development of ideas concerning the essence of living beings since it corresponds to the objective law of cause and effect relationships.

According to A. A. Lyapunov's definition [3], "life can be characterized as a highly stable state of matter which utilizes information coded by the state of individual molecules to evoke preservation reactions". This definition also emphasizes the functional aspect of life phenomena, which makes it possible to consider not only definite phenomena which we observe on Earth as life, but also to seek new forms of life beyond the Earth. In our study of life we are forced to rely on contemporary physical and chemical concepts, although we know they are insufficient for this purpose. Living systems, above all, possess the ability to preserve their physical and chemical properties in the presence of external influences. There are preservation reactions that are controlled by specialized control systems which receive certain information. Control systems must possess the ability to preserve information and to encode it effectively. A. A. Lyapunov considers that the stablest carriers of information codes are monomolecular carriers, and he defines living matter as being homogeneous, limited to 10^{-3}-10^{-4} mm, stable with respect to various external influences, and having preservation reactions and control systems. Living systems are macroscopic, multimolecular formations. There is an intensive exchange of information inside them; the transmission of information from one stable system to another during the process of evolution is characteristic (hereditary information).

The control systems of living organisms are multistaged and the adjustment of the lower levels is determined by the state of the higher levels. Evolution of the higher levels leads to an increase in stability due to the transmission of corresponding functions to the lower levels. A statistical relationship with the lower levels and, most of all, with objects inside the organism, is characteristic for the higher levels. This provides the requisite variety of preservation reactions. The statistical type of organization of the higher stage of control increases its reliability due to the easy interchangeability of lower-stage objects. Conversely, the structural relationships in the lower stages advance the problem of the reliability of control to a primary position.

The self-restoration of living structures is one of the important factors of reliability. Structural changes occur due to the influx of information and its subsequent processing. In the opinion of K. S. Trincher [4], living systems evolve over time in proportion to the logarithm of the information that continuously enters them during adaptation to the environment. But the preservation of an ordered dynamic structure entails the consumption of energy. A living system, therefore, may be considered as an open thermodynamic system. Work is accomplished as a result of the inflow of energy and the outflow of heat; this work causes a continuous structural break down of living matter at the temperature of life. A new thermolabile structure is simultaneously synthesized; the living system, therefore, can be said to be a machine which opposes thermal self-destruction.

Continuous structural restoration, i.e., constant rearrangment without cessation of its function, is a characteristic feature of a living system. This remarkable property is exhibited on the cellular and subcellular levels, while anatomical and physiological structures reconstruct themselves slowly /81 (embryogeny, growth, reproduction). Lower structures reconstruct themselves very rapidly, and restore themselves entirely. The study of the mechanisms of substitution, restoration, and self-repair of living structures is one of the central problems of contemporary biology. In the classical definition of life given by F. Engels, self-restoration of bodies composed of protein is noted as its chief quality. Another cardinal distinction of living matter should be noted at this time, i.e., the interchange of information. A living system is characterized by an exchange of matter [metabolism], energy, and information. The efficiency of a system drops during vital activity as a result of the accumulation of "errors". These errors are the result of incomplete compensation for losses related to the performance of work. In addition, distortions of information in the process of its transmission (noise) also lead to a decrease in efficiency. One of the causes of the accumulation of errors is the internal inertia of a living system since the majority of its component subsystems cannot respond quickly to all commands from the higher stage of control. Thus, there is an increase in entropy during vital activity. L. N. Plyushch [5] considers that the essence of life is a struggle with entropy. This definition opens up a wide perspective for analyzing life phenomena from the position of cybernetics and retains the applicability of thermodynamic laws to the evaluation of a specific class of reactions of living systems.

It should be mentioned that self-restoration processes in a complex living system are conditioned by information phenomena which are essentially controlling actions. The hierarchic organization of living systems makes extremely important the regulator mechanisms that increase the stability of the lower levels of the system by restricting their independence. In addition, it should be borne in mind that each level can have its own goal, and the goals can be antagonistic. Therefore, coordination at the higher levels, which is statistical in its essence, cannot be universal, and the transgression of individual elements beyond the systems' characteristic values (constants) is a frequent occurrence which leads to the accumulation of "errors" in the system. Living organisms as complex multigoal hierarchic systems [6] are organized entities. These organically complete systems [7] are made up of components which are subordinate to the organized entity in such a way that the qualitative distinctions between successively ascending orders of organization create the specific character of each level. The specific nature of the central organizer (higher level) determines the level and dynamic structure of the main active behavior forms of the organism as a whole, its inherent reaction norms exhibited during interactions with the environment, and the peculiarities of the organism's internal bonds and relationships [7]. /82

The concepts of structural and functional hierarchy of complex biological systems were the basis for the formulation of a number of theories of control in a living organism. The ability to homeostatically maintain the constancy of the internal environment as well as a dynamic, continuous balance with the external environment indicates that the systems of a living organism simultaneously deal with an enormous number of parameters. The information that proceeds to the control systems of an organism is truly colossal on all levels. Effective control requires, above all, an analysis of the information, then the development of the necessary solutions, and finally, the issuance of appropriate commands to the effectors. The interaction of the lower and higher levels of a complex biocybernetic system is based on an exchange of information via feedbacks which possess specific regulating thresholds. Autonomous traits are characteristic within certain bounds for lower levels. The system uses its available algorithms and generates corresponding expedient reactions as long as the information that proceeds to this level does not go beyond known limits. No messages are sent to the higher level at this time. Self-control, self-regulation, and self-monitoring characterize the work of each level of a complex system in the absence of unforeseen situations.

Interference at the higher levels in the work of the lower levels occurs only when the information flow exceeds the capabilities of the control systems. The appearance of any new, previously unknown signal significantly increases the entropy of a message, which is equivalent to a sharp increase in the volume of information transmitted over a communication channel. This entails the necessity of expanding the carrying capacity of the channel, which in turn lowers the interference stability of the system. Noise is also one of the causes of higher-level interference during the work of lower levels. Mutual interference among the elements of a living system is minimal under conditions of normal vital activity. It should be noted that noise is created mainly by the activity of adjacent elements of the system, since each one possesses its own algorithms and tries to solve its own problems without any concern for the others. This creates mutual interferences which, however, owing to the correlation established by interference at the higher levels (learning) or established during organization of the system (evolution), are below a certain threshold. The idea of independent /83 activity of individual elements of a biocybernetic system and their "egoism" in carrying out their particular programs is being developed by N. M. Amosov [8]. He writes: "....all programs of adjacent lower or higher systems that hinder the performance of a given system are interferences to it". N. M. Amosov defines principal and particular programs of a living system. Principal programs are realized not only by a harmonious combination of particular programs, but also by their contradiction. Cooperative and competitive relationships are possible between particular programs. Interferences arise as a result of competition. Interferences are factors which hinder the fulfillment of a given program.

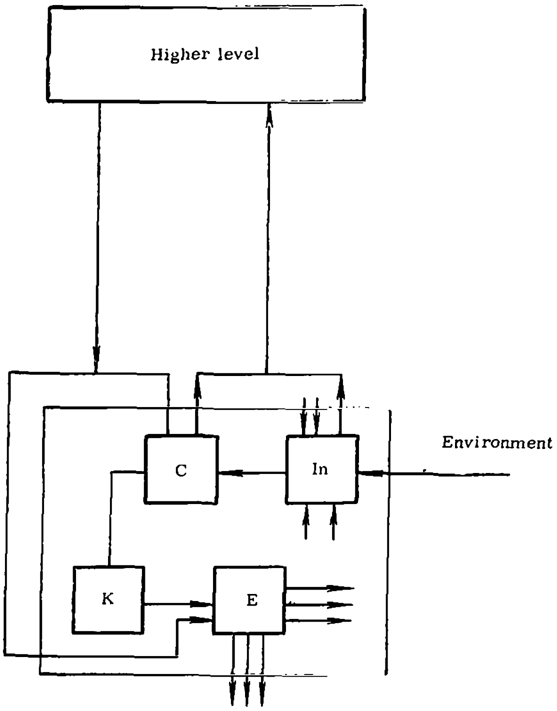

Figure 25. Model of a Two-Component Biological System. In = Inputs; C = Converters; K = Command Devices; E = Effectors.

The interactions of higher and lower levels of a biological system have attracted the attention of many scientists. It is sufficient to mention the work of K. M. Bykov's school on the study of the role of the cerebral cortex in the activity of internal organs [9]. The cybernetic approach to this problem makes it possible to introduce a quantitative interpretation /84 into observable laws, describe them mathematically, and simulate them. Let us consider a simplified model of a two-component biological system (Figure 25). One of the elements of this system is subordinate to the other. A cell, organ, physiological system, or entire organism may be such an element. An element of a lower level possesses the properties of self-regulation, self-monitoring, and self-control. These properties make up the basis of any living system [10]. The considered element of a living system must possess the necessary apparatus to realize these properties: devices for receiving and processing information, a control device which forms the appropriate commands, and effectors which carry them out. The considered element must receive information on both the internal and external environment, and its reactions must be directed internally as well as externally. The second component of the system, which is higher with respect to the one previously mentioned, has feedback with it. The feedback channel serves for monitoring purposes. Information obviously does not enter the monitoring channel under normal system operation (the information is equal to zero). On the other hand, the higher levels would suffer from an overload of information if the system was not operating normally. Recent research into the physiology of the reticular formation has indicated that the principle of selective sampling of the most important signals is extremely characteristic for the control systems of a living organism even on the highest level. The elements of the higher level interfere with the work of the lower level only when a lower element of the system cannot handle the information flow or cannot separate the useful information from the noise. Definite thresholds (dynamically regulated) must exist to determine the intensity of the information flow through the feedback channel.

Biology and physiology know of many examples of the transfer of control and regulation functions from a lower level to a higher level, while medicine uses this property of living systems in practice for diagnostic purposes. Thus, limiting parameters of the circulatory system are known in which the central mechanisms practically do not interfere with the processes of self-regulation and self-control. Even a slight load (physical or other) causes an active reaction of higher divisions. This reaction, however, is corrective up to a certain limit. The metabolism of the myocardium varies, the blood supply to the cardiac muscle varies, the contractile ability of the heart varies, and many parameters of the vascular system vary. All of these phenomena are directed toward the restoration of homeostasis. If the measures that are taken are /85 insufficient and the entropy of the system continues to increase, conditions arise for more active interference of the central mechanisms. This interference bears a controlling character, rather than a regulating one. The states of shock or collapse are examples of the action of central control mechanisms. This action is essentially a protective one with respect to elements of a higher level.

In connection with the considered interaction mechanism of the elements of a biological system, we should mention Selbach's work [11] on the principle of relaxation oscillations in the functioning of biocybernetic systems. The author considers that a system reverts to a certain initial state upon reaching an extreme limit related to expressed functional stress. This "reversal" is accomplished periodically in the process of homeostatic regulation, but its effect depends on the level of activity of the excited systems.

It is quite sufficient to establish three gradations for the parameters of a given element of a biological system in order to estimate the degree of its interaction with the elements of a higher level. The first limit can be called the monitoring level. Variations in the parameters of the internal and external environment that do not exceed this limit cause the arrival of a volume of information that is completely adequate for the natural control system of the given element. Self-monitoring, self-regulation, and self-control are accomplished in this case. Deviations in parameters that exceed the monitoring level cause information to flow through the feedback channel and signals to flow from the higher-level elements to the lower-level elements; the flow is addressed to the component of the self-regulation system which processes the information. If the corrective action of the higher-level elements on the algorithms of the lower-element activity is insufficient and its parameters reach the limit (the regulation level), there will be interference in the self-control process. It may be assumed that the arriving extraneous signals act directly upon the effectors and transfer the element in an extremely short period of time to a state which ensures survival of the system on the whole. Similar states are characterized by maximum subordination of lower elements to higher elements. From the standpoint of the games theory, the gain of the higher-level elements is one (1) and the gain of the lower-level elements is zero (0). Figure 26 schematically depicts the dynamics of a two-component biocybernetic system with the transfer to different interaction regimes of the elements. The states of the system above the control level are said to be threatening, and /86 characterized by a sharp increase in entropy, and lead to death. It is obviously expedient to distinguish one more level, the level of reversible changes, above which there occurs destruction of the system. Thus, the organism is above the control level for the first few minutes after clinical death, but below the level of reversible changes. As we know, modern medicine has the means to restore functions for 8 to 10 minutes after a clinical death, and this time is being continuously increased thanks to the efforts of scientists. It should be noted that the level of reversible changes is different for different systems. The activity of the cardiovascular system, thus, can be restored even one hour after death, while individual cells of a living organism continue to live for several days after clinical death.

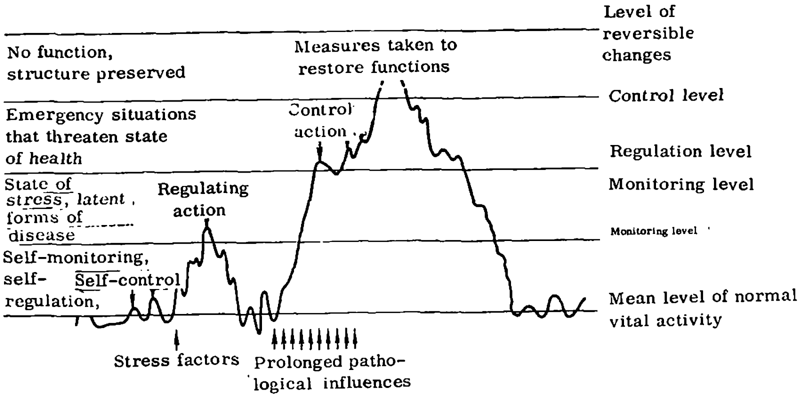
Level of reversible changes
No function, structure preserved
Measures taken to restore functions
Control level
Emergency situations that threaten state of health
Control action
Regulation level
Monitoring level
State of stress, latent forms of disease
Regulating action
Monitoring level
Self-monitoring, self-regulation,
Self-control
Mean level of normal vital activity
Stress factors
Prolonged pathological influences

Figure 26. Dynamics of the Interaction of Elements of a Two-Component Biological System Under Different Operating Conditions.

The above-considered principle of the interaction between elements of a biocybernetic system is universal for all levels of a living organism. The autonomy of the lower levels liberates the higher levels from the necessity of constant participation in local regulatory processes. In the transition from two-component systems to multicomponent systems, however, there arises a qualitatively new peculiarity of the biocybernetic system. The higher levels can perform their functions in this case only when the lower-level elements that unite them are mutually coordinated and act integrally in accordance with the /87 algorithm of the higher level. Interference and noise set in when the mutual coordination is disturbed, which is a warning that the higher-level elements are interfering with the activity of the lower-level elements. Centralization of regulatory phenomena is thus ensured with the autonomy of the individual elements retained. Centralized regulation provides for unity of the organism as a functionally complete structure.

Living organisms, especially the higher animals and man, are multicomponent biocybernetic systems. Various authors have proposed models of the general structure of the control system in a living organism.

S. N. Braynes and V. B. Svechinskiy [12] consider that the control structure in a living organism consists of three levels (Figure 27). The lower level

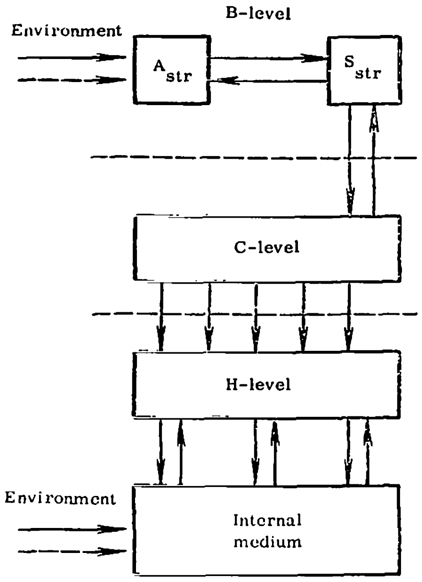

Figure 27. Three Levels of Control in a Living Organism [Braynes and Svechinskiy]. A_{str} and S_{str} = Types of B-Level Strategies.

forms the local systems that ensure the constancy of the physiological parameters in the norm. The second level optimizes the work of the first level by homeostatically changing it in accordance with the living conditions of the entire system. The main task of the second level is to find the optimum regime. The third level comes into play only when a situation arises in the environment which requires active readjustment of the work of the lower-lying levels. In this case, obviously, both the search regime and the limiting values of the parameters are changed. The authors give an example of an unsuccessful attempt made by Warner to create an automatic arterial pressure regulator. The failure resulted from the fact that the artificial control system, which had replaced one of the homeostasis systems, was not connected to the higher-level systems and, therefore, contradicted them.

Multiloop (multilevel) regulation in a living organism, which is based on the autonomy of individual elements and the centralization of control in the interests of the entire system, creates significant difficulties in experimental research on biocybernetic objects. The traditional isolation of the individual elements of a system in order to study their reaction to various factors which act separately contradicts the laws of the actual behavior of living organisms. At the same time, there were no methods available in the pre-cybernetic period for simultaneously analyzing the behavior of a large number of elements under the complex influence of many factors. The establishment of a common bond in the control systems of machines and living organisms makes it possible to use the advances of mathematics and engineering in biology and medicine. It is already clear, however, that the complexity of biological systems is such that fundamentally new mathematical methods (biological mathematics) and engineering methods (biological and medical electronics) must be developed. Thus, there arises the feedback in the "exact sciences -- biological sciences" system which is peculiar to cybernetics, where biology begins to exert a stimulating influence on the development of the exact sciences and, in particular, mathematics. /88

Biocybernetics of Cellular and Subcellular Structures

The investigation of the information mechanisms of the control processes in a living system is one of the most important tasks of biological cybernetics. The transmission of information, its processing, and encoding in the form of control commands are characteristic for any level of a living organism from the highest to the lowest. If the central nervous system and cerebral cortex form the higher level of a biological system, as it is usually considered, the question of a lower level in different periods in the history of science has been solved in various ways. The cellular level was the initial level not too long ago in all research on biology and medicine. Research was begun 10-15 years ago on the molecular level, which led to significant discoveries in the field of genetics and made it possible to create a new discipline -- molecular biology. The first biological research on the atom and electron level was the work of the famous biochemist, Szent-Györgyi, in the field of bioenergetics. His work led to the origin of one more exceptionally promising direction -- submolecular biology [13]. Szent-Györgyi pointed out that the interaction of molecular /89 structures and an electromagnetic field results in the excitation of electrons and their transition from one energy level to another. These energy reactions are closely related to biochemical reactions and, consequently, are information-conditioned, i.e., each electron transition is accomplished in accordance with a certain general program.

Szent-Györgyi's ideas have been the basis of some of the latest investigations in the area of information processes at the lowest (in the contemporary sense) level, i.e., the level of electrons, atoms, and molecules. The most complete and detailed account of the theoretical concepts on this problem is contained in the work of S. N. Braynes and A. I. Suslov [14].

The authors consider that control processes and the processes of information transmission and processing that are related to them in a living organism are composed of elementary acts of information transmission and processing which possibly occur on a molecular and submolecular level. In the authors' opinion, the elementary acts of transmitting and processing information are based on an energy exchange between specific molecular complexes by an electromagnetic field. Using Szent-Györgyi's propostion concerning coupled oscillators [15], they suggest that the interaction between molecules may be accomplished at distances less than a wavelength of electromagnetic emission or comparable to it. Two molecules whose electrons can be identically excited are able to behave as coupled oscillators. The energy imparted to one group of electrons in this case can be used by any other group. The hypothesis concerning an information exchange between complexes of biological macromolecules by means of an electromagnetic field was also advanced by Norbert Wiener in connection with the mechanism of genetic processes in a cell [16]. Polonsky [17] considered the DNA molecules in a cell as electromagnetic-signal generators, the RNA molecules as amplifiers, the amino acids and enzymes as effectors, and the cell membranes as noise filters.

In the opinion of S. N. Braynes and A. I. Suslov, there are networks in biological structures that consist of oscillators which process information. The networks overlap and are frequency-separated. The networks are similar to a three-dimensional lattice whose nodes contain oscillators and possess the property of periodicity. Each network interacts with an electromagnetic field and generates oscillations of a definite frequency. As indicated by I. M. Gel'fand and M. L. Tsetlin, a hypothetical medium that consists of elementary /90 oscillators is able to perform logical actions and memorize information [18].

The performance of the elementary acts of information transmission on a quantum level in the presence of quantum amplification satisfies the requirement of small information losses in these acts. Considerations of ensuring the necessary interference-stability compel us to think that the quantum transmission of information occurs in the infrared range of the spectrum. It is possible that the transmission of signals from receptors to centers through nerve fiber is similar, to a certain extent, to the propagation of a field in a dielectric waveguide quantum amplifier.

Consideration of information transmission as interactions between an electromagnetic field and specialized biological structures in the form of networks made up of oscillators of various frequencies opens new possibilities for the experimental study of biological subcellular structures. There is no doubt that the key to the "secrets" of the control processes in biological systems will be found precisely in the field of molecular and submolecular biocybernetics. The study of the elementary acts of information transmission will enable us to secure a deeper understanding of the laws observed at the higher levels of a living system.

The development of biocybernetics of subcellular and cellular structures has made it possible to perform an informational analysis of metabolism processes, which entails the encoding of information in the form of stationary concentrations of components of an open biological system that participate in a network of chemical transformations. A. G. Pasynskiy [19] considers that the sequence of actions and reactions forms an extremely branched, but strictly organized, network. There is no substance in the organism that could not enter the composition of this network of reactions -- on its linear sections between nodes, in the lateral branches, on its ends, or even on the branch nodes. Changes occur in the stationary concentrations of components of a system when the external conditions, temperature, or composition of the medium are changed. This essentially denotes a recoding of the information received from the environment into a set of stationary concentrations. The presence of cellular membranes has a significant effect on the stationary concentrations. The permeability of biomolecular structures of a number of cellular membranes can change sharply under the influence of insignificant amounts of hormones and various mediators.

It is important to note that the encoding of external information in the form of a set of stationary concentrations occurs independently of the code of the information included in the nucleoproteins. It is very probable that the mechanisms of biological information, which are related to the stationary concentrations and membranes, are more ancient than the mechanisms related to the nucleoprotein molecules. Stationary concentrations possess the ability to change continuously in distinction from discrete structural codes. /91

An important role is played in biochemical transformations by the feedback which arises due to the mutual influence of the rates of formation and consumption of reacting substances. The concentration of intermediate products influences the quantity of enzyme or catalyst [20]. For example, inorganic phosphate and adenosine diphosphate (ADP) are the key substances of the regulation process in the energy-transformation cycle of adenosine triphosphate (ATP). The concentration of these substances increases when the ATP is consumed, which in turn increases the rate of anaerobic and aerobic cleavage of a number of organic substances. An increase in the speed of these processes, however, leads to a decrease in the ADP and phosphate concentration due to the consumption of these substances in the formation of ATP. This in turn lowers the rate of respiration and enzymatic decomposition. The more intense the work of an organ, the more intense the ATP cleavage. An increase in the quantity of ADP and phosphates creates favorable conditions for resynthesis of ATP since ADP is converted into ATP in the presence of a mineral phosphate during vigorous respiration. In this case there is a typical system with feedback, where the build-up of decomposition products of certain substances creates the conditions for their removal by means of reverse synthesis [21].

Any physiological reaction is accomplished by means of a coordinated series of chains of biochemical reactions. The entire network of biochemical reactions in an organism undergoes continuous subtle changes which adapt the organism to the continuously changing external conditions. The control process in the organism consists in a search for the most optimum functioning mode. This mode automatically coordinates the branched network of biochemical reactions with the other biological processes.

Protein synthesis is one of the most important biological processes that take place in any biological system. This process is the basis for the flexibility of functions; it ensures the restoration of functioning energy-forming, supporting, and other structures of differentiated cells, and is necessary for maintaining their physiological function under the conditions of the entire organism [22]. The energy accumulated in the phosphate bonds of ATP and the decomposition products of carbohydrates and other substances are used for protein synthesis. Protein synthesis, in turn, ensures the influx of proteins and /92 enzymes which are necessary for energy formation and development of the structures in which these processes take place. Protein synthesis is accomplished by the genetic apparatus of differentiated cells and is currently the subject of intensive research.

The genetic apparatus of the cells plays a leading role in hereditary phenomena. The genetic information of organisms, which is created in the process of evolution, is encoded in the molecular structure of desoxyribonucleic acid (DNA). The DNA molecules in a cell are united into supramolecular micellar structures -- chromosomes. Chromosomes are components of the cell nucleus. The gene as a material hereditary subtratum was only a speculative concept for a long time. Then, after detailed investigations of the structural rearrangements in the chromosomes, the gene concept became identified with their material loci; and the linearly arranged centers which, upon closer study, were clusters of many hundreds of nucleotide pairs united into chains of DNA polynucleotides, were considered to be genes.

Research on the fine structure of genes led to the deciphering of the genetic code and an explanation of the relationship between the DNA structure and the gene properties. The work of Watson and Crick, which was published in 1953, was the beginning of this research [23]. Their work established the general plan of the DNA structure and suggested a mechanism for its reproduction in an organism.

It is known at this time that information on the synthesis of certain proteins is recorded in nucleic acids by a triplet code, i.e., each amino acid is determined by a combination of three nucleotides. Several triplets correspond to each amino acid and the triplets follow one another in a definite sequence. There are no dividing sections between the triplets, and they can be correctly counted only by means of the strict fixation of the "beginning" of the count. The composition of nucleic triplets has already been deciphered for all known amino acids (Table 3).

Further research made it possible to explain the mechanism that transmits the information which is encoded in nucleic acids. Protein synthesis is accomplished in special cellular structures, i.e., ribosomes, which contain ribonucleic acid (RNA). The information contained in DNA is transmitted to RNA through M-RNA, which is the intermediary. M-RNA is synthesized into DNA as in a matrix. The entire DNA structure is not copied in this case, but only individual portions of it. The read-out of information from DNA by means of M-RNA is regulated by the cytoplasmic products or products of the medium which activate /93 the various RNA-repressors, i.e., special RNA fractions.

TABLE 3. AMINO ACID TRIPLET CODE

Phenylalanine	UUU
Alanine	UCG
Arginine	UCG
Aspartic acid	UAG
Aspargine	UAA, UAC
Cysteine	UUG
Glutamic acid	UAG
Glutamine	UCG
Glycine	UGG
Histidine	UAC
Isoleucine	UUA
Leucine	UUC, UUG, UUA
Lysine	UAA
Methionine	UAG
Proline	UCC
Serine	UUC
Threonine	UAC, UCC
Tryptophan	UGG
Tyrosine	UUA
Valine	UUG

Nucleotides: U = Uracil; A = Adenine; G = Guanine; and C = Cytosine.

Thus, cellular metabolism renders a direct influence on DNA by determining its working areas and intensity of protein synthesis. In the opinion of A. S. Spirin [24], only that which must be synthesized is recorded in DNA, but there is no information on the direction of development. Desoxyribonucleic acid is only a book that contains everything of use to the organism in various periods of its life. There is still another special mechanism which makes it possible to correctly read this book, i.e., the necessary pages at the necessary moments. This mechanism is evidently determined by the general structural-chemical organization of the cell and the cytoplasm--nucleus system.

Protein synthesis in a cell is directly related to energy transformation and the provision for functional stability of the biological structure. The rate of protein synthesis should correspond to the rate of functioning and wearing-out of the structures. F. S. Meyerson [25] has advanced the concept of the presence of a bond between the genetic apparatus of a cell and its physiological function. The experimental study on the effect of the physiological activity level of an organ on the synthesis of nucleic acids and proteins has made it possible to establish a number of important laws and has led to the concept of the functioning rate of structures. The structures' functioning rate /94 is equal to the ratio of an organ's function to the mass of its functional elements and can be conditionally expressed as the number of functions performed by a unit mass of the organ per unit time. It has been established that the compensatory hyperfunctioning of vital organs (e.g., the myocardium [26]) leads to hypertrophy in connection with an increase in the structures' functioning rate, which activates protein synthesis and thus brings about an increase in the cellular mass of the organ. Hypertrophy of the organ leads to a distribution of this accelerated functioning into the regenerate functioning elements, i.e., to a decrease in the functioning rate of the structures and the cessation of further hypertrophy, respectively. The genetic apparatus thus changes its activity as a result of obtaining information on the change in the level of functioning and wearing-out of the structures. This information, which is sent from the cytoplasm to the nucleus and indicates the level of physiological functioning, plays the role of feedback and regulates the activity of the genetic apparatus.

Protein synthesis occurs in an organism that is already formed, as well as in all stages of its development. The individual development of an organism begins with the transfer of genetic information placed in the chromosomal DNA to the protein synthesis taking place in a living cell. The genetic information is transmitted through the DNA -- M-RNA -- RNA channel and thus ensures the formation of specific protein molecules. This information directs and monitors the synthesis of the chemical substances and the rate of the various reactions during the metabolic processes. The autoreproduction ability of the DNA molecules and chromosomes is an extremely important material factor in the transmission of hereditary information. Mutations occur in the process of transmitting hereditary information under the influence of external and internal causes, i.e., deviations in the given DNA code of structural and functional organization. From the standpoint of information theory, the appearance of mutations is equivalent to the appearance of noise in a communication channel, and leads to errors in information transmission. The accumulation of errors in a genotype leads to a breakdown in the structure and function of a biological system and, if the errors are serious and numerous, to the death of a living system.

Along with the accumulation of errors, there also occurs the selection of the most viable objects, which creates favorable possibilities for opposing various external influences (the interference stability of the systems is increased). As we know, one of the ways of increasing interference stability consists in creating redundancy of the information to be transmitted. It seemed /95 that the correction of errors during the transmission of genetic information would be ensured as a result of an excess of structural information. The amount of redundant information in an organism, however, is limited to a volume which provides for a minimum of errors compatible with the further existence of the organism but not enough to completely eliminate the errors. This proposition has been called Dankov's principle [27]. Errors accumulate during the developmental and life processes of an organism, thus bringing about the aging process. Aging is accompanied by a change in the physical properties and chemical composition of the tissues, organs, and cells, but the destruction of homeostatic mechanisms is primary in these changes [28]. It is the result of a disruption of information. Information redundancy is the basic weapon of a living organism in its struggle with aging. As several investigations have indicated, biological systems possess a six- to eight-fold information redundancy. Thus, an entire organism can be obtained from separate cells taken at the stage of a 2-, 4-, or even 8-cell embryo, but imperfect embryos are obtained from the 16- or 32-cell stage.

The mutual exchange of information is the basis of the organization of the individual elements in a complete organism. Information processes ensure the reaction of subcellular structures as a single system. A cell is a complex biological object. Metabolic processes take place in it continuously, thus maintaining the internal submicroscopic structure; and, conversely, the organization of metabolic phenomena is ensured only by the completeness of the structural supramolecular ensemble [29].

A cell is a complex of self-regulating adaptations, a self-adjusting unit set up for optimum operating conditions. We have already examined the mechanism for regulating protein synthesis; it is based on the interaction of the nucleus and cytoplasm with the presence of direct communication and feedback between them. Feedback also characterizes other reactions in a cell. The biochemical processes related to the activation of enzyme systems which function as an operational adaptation of a cell to rapid changes in the internal and external medium, for instance, also are based on feedback mechanisms. Along with the direct reverse effect of the product on the final and intermediate links of the entire enzyme chain, the feedback of the final product with the very first key link of the enzymatic reaction is also used. Depending upon the concentration of the final product, this link can stimulate or suppress the enzymatic acti- /96 vity [30]. Figure 28 illustrates a diagram of the work regulation of a multienzyme system by the product via a negative feedback mechanism. The ability of certain enzymes to receive information on the volume of work performed by them is the basis of control and self-regulation in multienzyme systems.

The activity of a cell on the whole is determined by its continuous self-adjustment to a new, "optimum" operating mode. A cell is able to mobilize its chemical power at a certain moment and can guide the consumption of energy in a certain direction. One of the important instruments of the regulatory adaptation of a cell is its structural mobility. The absence of stability in cellular structures and their continuous changing was detected by the interference optical method in G. M. Frank's laboratory [29]. It is assumed that structural variations are related mainly to the rhythmic activity of mitochondria. The rhythm of submicroscopic mobility, as investigations have indicated, coincides with the rhythm of oxidation. An assumption has been made that these rhythmic oscillations are external expressions of the work of regulatory mechanisms.

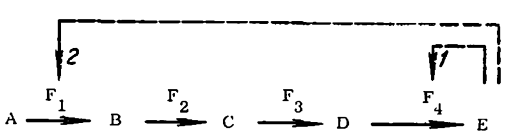

Figure 28. Diagram of the Regulation of a Multienzyme Biochemical System (Cafiani). A, B, C, D, and E = Initial, Intermediate, and Final Products of an Enzymatic Reaction; F_1, F_2, F_3, and F_4 = Enzymes; 1 and 2 = Feedback of Final Product with the Final and Intermediate Link of the Reaction.

A living cell possesses a large number of hierarchically interrelated mechanisms. It is a system which is significantly more complex than we can imagine at the present time. Its complexity is dynamic and, because of this dynamic nature, the work of a cell is extremely reliable under the most diverse conditions. There is no doubt that the probing into the "secrets" of the cell in the near future will result in some significant discoveries in the field of biology and will be of much interest to engineers who are concerned with problems of reliability.

Cybernetics of Physiological Systems /97

As we know, physiology is concerned with the study of an organisms's activity on the whole, its various functions, and the physiological mechanisms that unite and regulate the work of organs and systems.

Physiology is a branch of biology which is closely related to the other biological sciences, physics, and chemistry. F. Engels wrote: "Physiology, of course, is the physics and, in particular, the chemistry of a living body; but, at the same time, it is a special form of chemistry, on the one hand, as its sphere of action is limited here; but, on the other hand, it rises to a higher level" [1]. The laws of a biological object on the level of physiological systems are more difficult to explain from the standpoint of physics or chemistry than on the cellular and subcellular level. Highly specialized mechanisms which have an expressed peculiarity within each physiological system occupy the prime position here.

The concept of a physiological system includes the functionally complete organization of a number of anatomic-morphologic formations which perform a specific task. Speaking in the language of cybernetics, a physiological system is part of a living organism (structurally united or separate) inside of which there takes place an exchange of information on the basis of a general algorithm.

The physiological systems of an organism, in turn, are joined together to form a single higher-order system, i.e., a complete living organism. The process of the gradual complication of biological objects by means of building on

newer levels of regulation, which is brought about by evolution, led to the emergence of organisms with various types of multilevel regulation. N. M. Amosov [8] distinguishes four types of regulating systems. The first was conditionally called the chemical, or nonspecific, system; it provides for the interaction of organs through metabolic products. The second system is the endocrine system. It activates various organs by secreting special substances, i.e., hormones. The third regulating system is the autonomic nervous system. The principle of local nerve action is the same as in the first two systems, i.e., chemical, but remote operational control is accomplished here from one center simultaneously for several objects: organs, tissues, physiological systems. The fourth regulating system is the brain and the central nervous system. The brain, on the one hand, performs higher functions to maintain the /98
stability of the organism's internal medium (homeostasis), and on the other hand, it performs the function of balancing the whole organism with the external medium.

The interrelationship between the physiological systems of an organism ensures adequate responses to various influences under normal conditions. The common bond between all of these responses consists in balancing the system of an entire organism by means of bringing it to a stationary regime. In our opinion, biological processes can be divided into two types: stationary and transient. B. V. Gnedenko, S. V. Fomin, and Ya. I. Khurgin [32], in addition to these two types, also distinguish pulsed random processes. They are, however, evidently a variety of the transient processes, peculiar to systems with rapid attenuation or with a short build-up time. Build-up time, as one of the characteristics of a physiological system, must be different in different systems. Some systems (e.g., several elements of an encoder) change over from one level to another very slowly, while others (e.g., nerve centers) change over very quickly. Each physiological system can be observed in two different states -- stationary and transient. The stationary states are characterized by ergodicity, i.e., a variable quantity which reflects certain peculiarities of a given system, and varies in such a way that the time averaging corresponds to the set-realization averaging. In other words, fluctuations can be considered as a stationary random process. An example of a stationary random process is a dynamic series of RR intervals in the electrocardiogram of a human being at rest, or the electromyogram of thigh muscles in a standing position, or the motion parameters of a runner in the middle of a race. The statement "in the middle of a race" is very essential in the last example. It emphasizes the existence of a steady-state regime as distinct from the transient characteristics that are observed in the starting period and at the finish line. The stationary characteristics of various physiological parameters can be expressed in different ways. For example, the stationary state of the circulatory system in physiology and clinical medicine is usually characterized by the average pulse rate. Cybernetics provides the possibility for a deeper penetration into the essence of stationary physiological processes. It is known, for instance, that the stationary states of a conditioned athlete in an ordinary working situation and an unconditioned individual in a state of sleep are not equivalent, even though their average pulse rate may be the same.

Chapter III considers various methods for the mathematical analysis of /99
physiological processes, including means for computing the autocorrelation func-

tion, constructing variation curves, etc. These methods make it possible to more deeply characterize stationary states and to evaluate them mathematically, which then permits a detailed quantitative investigation of the homeostatic mechanisms of a living organism.

Transient states are the moments when a physiological system changes over to a new stationary regime. All regulating systems participate in transient processes to some extent. A transient process is the organism's response to an external influence. In a narrower sense, it is the response of a given physiological system to a disturbance that is external for it (but not for the entire organism). For example, the respiratory variations during the cardiac cycle may be considered as transient processes in response to disturbances brought about by respiration (see below). The peristaltic movements of the intestine may be considered as responses to mechanical stimulation. A stationary regime thus includes a series of transient states. A transient regime, in turn, consists of stationary portions. One of the specific features of a biological object consists of this dialectic unity and contradiction of the stationary and transient states of physiological systems. Figure 29 illustrates examples of stationary and transient regimes of the circulatory system in the form of cardiointervalograms recorded immediately after exercising.

The role of the transient processes consists in constantly balancing the individual physiological systems with respect to optimum adjustment of the organism as an integral system. Therefore, a transient process in one of the physiological systems leads to the appearance of transient processes in the other systems. The interrelationships between stationary states then change correspondingly. The mathematical dependences between individual parameters of various physiological systems are called transient functions. These functions, however, are obviously different for stationary and transient regimes.

The comparison of engineering and biological systems has led to the development of new methods for analyzing transient characteristics in biology. All changes in the state of biological systems can be classified as compensatory changes or as changes related to the disturbance of regulation caused by a damaging influence. The flexibility of biological systems and their high reliability even in the case of damaging influences can ensure the needed level of /100 regulation owing to duplicating control loops or by means of the inclusion of new control systems (the formulation of new programs).

The method of introducing certain experimental disturbances can be used to investigate biological regulators by analogy with engineering systems. By observing the regulation process in this case, conclusions can be made concerning its quality and possibilities. Physiologists have been using this method in practice for some time already, but the cybernetic approach provides for a precise quantitative evaluation of the work of biological regulators. Pathological and clinical physiology provide the richest material for studying the work of various biological regulation systems. Functional tests, therapeutic measures, the evolution dynamics of a disease and its subsequent cure can be interpreted precisely and quantitatively if the principles of automatic regulation theory are utilized.

G. Drishel' [33] formulates the basic proposition concerning the analogy /101

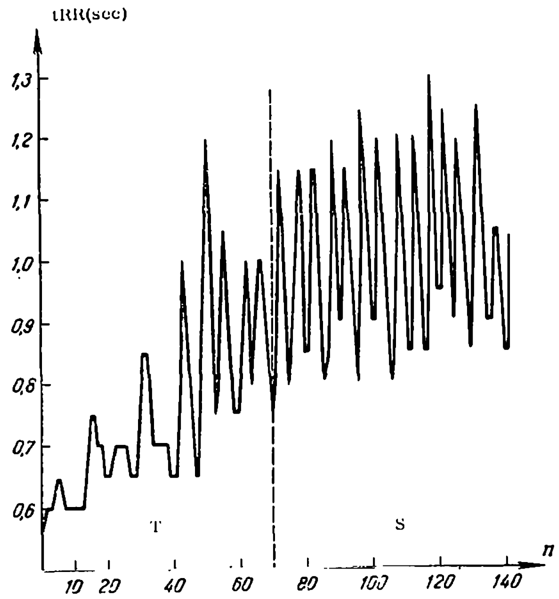

Figure 29. Cardiointervalogram After Physical Exercise. Transient Operating Conditions are Shown on the Left of the Dotted Line (T). Steady-State Conditions are Shown on the Right (S).

between biological and engineering automatic-regulation systems in the following way: "The character of periodic regulation processes in biological systems is analogous in principle to the behavioral character of engineering regulation systems. In both cases the former or a new equilibrium state is achieved after deviation of the quantity to be regulated from the equilibrium state as a result of an oscillatory process which, depending upon the properties of the system, can be an aperiodic or periodic attenuating process, i.e., it bears an exponential or sinusoidal character in first approximation". In the opinion of G. Drishel', the quality of regulation in biological systems can be evaluated according to the "regulation area", which is the area of a closed region that is bounded on one side by the line of the equilibrium state and on the other by the curve of the transient process. The smaller the "regulation area", the higher its quality. Optimum dynamic characteristics of biological regulation systems correspond to minimum "regulation areas". Deviations are possible from optimum adjustment toward periodic or aperiodic "degeneration" of regulation, depending on the characteristics of the transient process. The experimental determination of the transient processes in biological regulation requires the use of proportioned actions of normal magnitude (i.e., within the limits of physiological loads which can be withstood without damage), whereby the system under investigation should be in the initial equilibrium state. The function being investigated is continuously recorded to evaluate the quality of regulation. Various time characteristics are measured to determine the dynamic type of regulating system: latent periods, maximum deviation time, etc.

Physiological cybernetics arose and is being developed at the present time. It is a new discipline which unites the physiological work analysis of certain functions and the cybernetic analysis of them as information processes related to the optimization of control. Physiology must know, above all, the parameters of the main physiological systems of the living organism in the form of quantitatively expressed mathematical laws which characterize normal steady-state and transient processes. Simulation of these processes with the aid of analog and digital computers will open the way to further penetration of the secrets of living nature and will essentially improve diagnostics owing to the rapid manifestation of indices that do not correspond to the given model. Disease mani- /102
festations are characterized by other steady-state and transient conditions and,

consequently, by other models. Chronic diseases are new interrelationships between physiological systems which have been organized in the course of adapting to certain influences and which ensure a new, sufficiently stable, level of functioning. The model of this level should have a mathematical expression of a steady-state process. Conversely, acute diseases should be characterized by models which have the form of transient processes. Thus, knowledge of the models of various steady-state and transient conditions of physiological systems would make it possible to rapidly and accurately diagnose diseases and to evaluate the functional status of the organism. Today we are still very far from establishing physiological cybernetics as a new division of biological science; however, the prerequisites for it in the future are already present. Most of the research done recently in our country and abroad has been in the area of cybernetic analysis of certain physiological reactions. Later, we shall give only a few of the examples which indicate the possibilities of applying cybernetics in various areas of physiology.

Regulation of the Cardiac Rhythm

The existence of respiratory variations in the various circulatory indices has been known for some time. Respiration renders a noticeable influence on the heartbeat. This influence is accomplished chiefly through the vagus system. Kleins [34] computed the "respiration -- vagal inhibition" transfer function:

$$\frac{S^2}{(1 + T_1S)\ (1 + T_2S)}$$

where $1 < T_1/T_2 < 4$; $T_{1,2}$ are the time constants (the first and second phases of the respiratory reflex), and S is the Laplace operator. The transfer function makes it possible to predict the pulse rate very well on the basis of the respiration rate. Experimental research has indicated a 0.93 degree of correlation. Local mechanisms (self-regulation) as well as higher divisions of the central nervous system (control) participate in regulating the heartbeat. Tonus variations of the vagus nerve, which affect the magnitude of the threshold potential and the depolarization curvature of the sinoatrial node, and also affect cell membrane permeability and the ratios of potassium and calcium ion concentrations, play a prime role in the first regulatory system. This leads to a change in the length of the cardiac cycle (Figure 30). /103

The average pulse rate depends on the part of the sinoatrial node in which the pacemaker is located. The pacemaker is a group of cells which control the self-oscillatory process. The cells located in the upper part of the sinoatrial node possess increased irritability and provide a higher pulse rate in the role of the pacemaker. When the vagus nerve is stimulated, the "initiative" of the cells with high irritability is suppressed and the role of the pacemaker changes over to the cells located in the middle or lower parts of the sinoatrial node. As a result of the reflex action of respiration on the tonus of the vagus nerve, periodic changes occur in the position of the pacemaker in the sinoatrial node which are synchronized with respiration, or to be more exact, with the respiratory oscillations in tonus of the vagus nerve. Thus, the signals generated by the sinoatrial node are modulated, as it were, by processes associated with respiration. The activity of the sinoatrial node in this case can be thought of as being adaptive and brought about by the compensatory reaction of the heart to the action of factors associated with respiratory movements: the variation in blood inflow and outflow, pressure variation in the thoracic cavity, etc. From the standpoint of the self-regulating system of the sinoatrial node, respiration may be considered as a disturbance, a noise, or an interference. /104

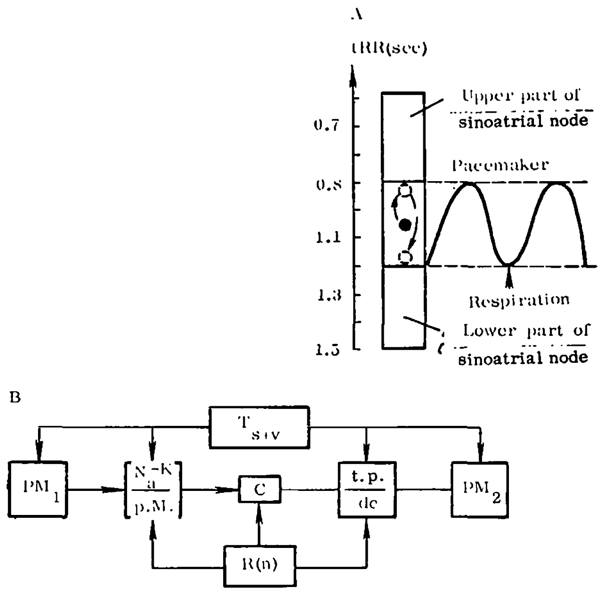

Figure 30. Self-Regulating System of the Sinoatrial Node. A = Variations in the Pacemaker Position in Association with Respiration; B = Block Diagram of the Sinoatrial Node Information Control System; $PM_{1,2}$ = Cells = Pacemakers; Na-K = Concentration of Sodium and Potassium Ions; p.M. = Cell Membrane Permeability; t.p. = Threshold Potentials; d.c. = Depolarization Curvature; C = Communication Channel; T_{s+v} = Tonus of Sympathetic and Vagus Nerve; R(n) = Respiration (Noise).

A decrease in sinus arrhythmia during physical exercise, following an injection of atropine, or after inhaling amyl nitrite, may be interpreted as the process of optimizing an information system, which leads to an increase in its reliability. The frequency band of the information channel becomes narrower in this case.

The second control loop for the heartbeat rhythm ensures the admission of regulating (correcting) and controlling signals from the central nervous system. There are two paths for extracardial influences on the heart: neural and endocrine (humoral). The information transmitted humorally is of importance for ensuring the necessary operating level of the cardiovascular system. The "commands" transmitted humorally, however, are characterized by delayed transmission. The effectiveness of the humoral channel is lower than that of the neural channel, although its interference-stability and reliability is higher because of the more improved encoding of information.

Control via the sympathetic and vagal systems evolved later than control by way of the humoral channel. Its purpose is to ensure operationing reactions to various external influences of a primary or brief character. Stable adaptation to varying environmental conditions is accomplished by means of "humoral" commands which proceed to the heart and to the sinoatrial node following the "nerve" commands. The "nerve" commands in this case bear a preliminary character in some instances and lay the groundwork for optimum reception of the main, effector command which comes over the humoral channels. Duplication of commands and separation of the preliminary and effector command are obviously also mechanisms for increasing the reliability of a control system.

Considering the humoral commands that are sent to the sinoatrial node, it should be noted that the dynamics involving hormonal secretion into the blood can essentially affect the heartbeat rhythm. Thus, the influence of the thy- /105 roid gland hormone on pulse rate is well known. Tachycardia is observed in Basedow's disease and bradycardia is exhibited in myxedema. An injection of adrenalin is analogous to the stimulation of the sympathetic system. Hormones affect not only the pulse, but also other physiological functions.

A great deal of interest has recently been exhibited in the slow rhythms of the organism: the minute and hourly rhythms. They are considered to be related to the activity of the neuro-endocrine apparatus [35]. Rats have temperature rhythms with a periodicity from 1 to 4 hours [36]. Slow fluctuations in pulse and arterial pressure have been detected in cats and rabbits [37, 38]. Special investigations have indicated that humans exhibit rhythms with a periodicity from 2-3 to 30 minutes while at rest, and there probably are even longer "rhythms". It is very tempting to work out a procedure for studying the neuroendocrine apparatus on the basis of slow heartbeat rhythms. This is quite realistic in a theoretical sense. The extraction of a maximum of data from a minimum of information is one of the tasks of cybernetics.

Regulation of Respiration

Much work has been devoted to problems of the cybernetic study of the various aspects of the respiratory process. Grodins [39] considers the gaseous components (pO_2 and pCO_2) of arterial blood as the regulated object, and the respiratory center and pulmonary muscles as the regulators. The metabolic production of CO_2, the CO_2 content in inhaled air, and pulmonary ventilation serve as variable systems. The dependence between these indices is described by third-order nonlinear differential equations. An analog computer can be used to investigate the transient characteristics of ventilation and the arterial CO_2 concentration.

Rashevskiy [40] also describes the dependence between the indices of the respiratory system by means of differential equations. The process of oxygen diffusion from the cavity of a pulmonary alveolus into the capillaries is expressed by the following equation:

$$V de/dt = - Sh(e - cb),$$

where V is the volume of the alveolus; de/dt are the variations in the O_2 concentration in the alveolus during the diffusion process; S is the surface of the alveolus; e is the oxygen concentration in alveolar air; cb is the O_2 concentration /106 in the blood; h is the permeability factor of the alveolar epithelium and the capillary walls for O_2. The rate of admission of O_2 into the alveolus from the external air is equal to Ca•dv/dt, where Ca is the O_2 concentration in inhaled air, and dv/dt is the change in volume of the alveolus. The expression d(Ve)/dt indicates the rate of change of the O_2 mass in the alveolus. The entire process of oxygen exchange in the alveolus is described by the following equation:

$$d(Ve)/dt = Ca\,dv/dt - Sh(e - Cb).$$

The total amount of oxygen that is diffused into the blood in one respiratory cycle (q) can be expressed in the form of the sum of two integrals:

$$q = sh\int_0^{at}(Ci - Cb)\,dt + Sh\int_0^{(1-a)t}(Ci - Cb)\,dt,$$

where t is the duration of the respiratory cycle; at is the inspiration time; (1 — a)t is the expiration time; Ci is the oxygen concentration in the alveolar air and in the inspiration period; Cb is the oxygen concentration in the alveolar air in the expiration period.

Simpler mathematical expressions for simulating the respiratory system were proposed by Horgan and Lange [41]. The authors propose that the partial pressure of carbon dioxide, oxygen, and pH of the arterial blood are the only factors which control ventilation. The pulmonary system can be represented in the form of two equations which characterize the admission, excretion, and accumulation of O_2 and CO_2 in the lungs:

$$CvCO_2 - CaCO_2 = \frac{100}{Q_c(Pb - 47)}\left[VaPaCo_2 + \frac{d}{dt}/FRC \cdot PaCO_2\right]$$

$$CaO_2 - CvO_2 = \frac{100}{Q_c(Pb - 47)}\left[Va(PiO_2 - PaO_2) - \frac{d}{dt}FRC \cdot PaCO_2\right],$$

where $CvCO_2$, $CaCO_2$, CvO_2, and CaO_2 are the oxygen content and carbon dioxide content in the venous and arterial blood in percent; $PaCO_2$ and PaO_2 are the partial carbon dioxide and oxygen pressures in the alveolar air in millimeters of mercury; pCO_2 is the partial oxygen pressure in the inhaled air; Pb is the barometric pressure; Qc is the blood flow rate in liters per minute; Va is the alveolar ventilation in liters per minute; FRC is the functional residual capacity of the lungs in liters.

As we know, animals with constant body temperatures are said to be homothermal. The lowest temperature is characteristic for lower mammals. The temperature of the other mammals is between 32 and 40°. The body temperature of birds is 40-42°. The accuracy of regulation fluctuates from several degrees to a tenth of a degree. Average body temperature in humans is 37°, and the accuracy of regulation is ±0.1°. G. Hansel's detailed work is devoted to problems of regulating body temperature. Figure 31 illustrates a diagram of Hansel's system of body temperature regulation. Table 4 lists the main regulating actions.

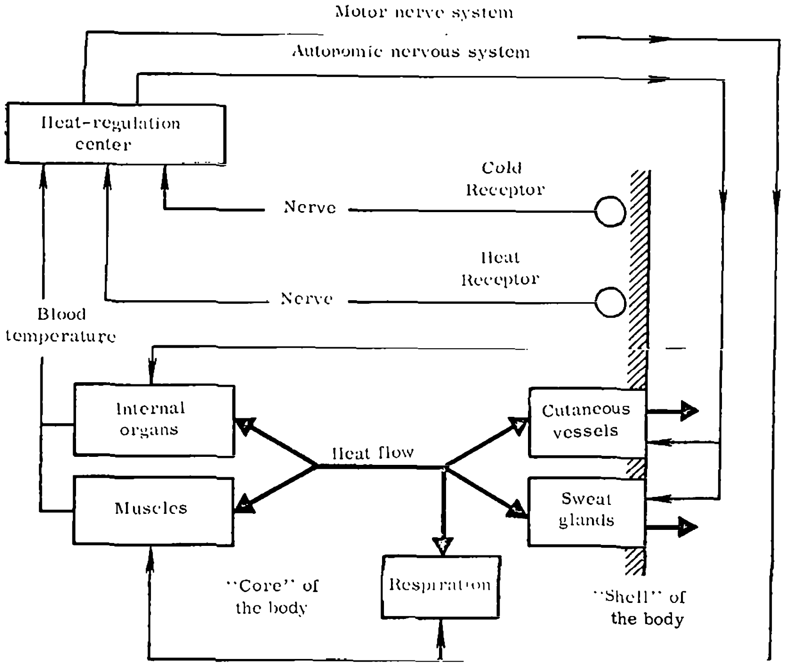

Figure 31. Diagram of Temperature Regulation (G. Hansel).

The heat receptors, which are located in the skin, introduce signals of external disturbances (heat, cold) into the heat regulation center. A corresponding quick reaction of the system maintains the internal temperature at the given level. The particular nerve formations located in the hypothalamus are /108 the measuring elements of the system. In addition, they are closely associated with the periphery by means of sensory and motor nerves. The heat regulation center carries out programmed temperature regulation according to the time of day (average body temperature in the morning is 36.5°, and 37.5° in the evening). In the case of disease, an increase in body temperature involves the readjustment to the operational program of the heat regulation system to maintain a higher temperature level. Disturbances in heat regulation may occur as a result of an action that is immediately directed to the regulatory organs. Thus, when persons under the influence of alcohol become chilled, the cutaneous blood

TABLE 4.

Heat Production	Heat Emission
1. Oxidation in the muscles:	1. Change in size of body surface
a) during involuntary movements (trembling)	2. Change in position of hair
b) during voluntary movements	3. Perspiration
2. Oxidation in the internal organs	4. Hurried breathing
	5. Blood flow changes in skin

vessels relax and the pressor commands from the heat regulation center cannot be executed. Due to this, intense heat emission occurs through the skin. A human being in this condition receives the impression of heat, whereas in actuality a sharp cooling of the organism takes place.

Regulation of Blood Sugar Level

Detailed experimental investigations of the glucose-insulin system based on the quantitative measurement of various parameters have made it possible to advance a number of hypotheses concerning the processes for regulating the blood sugar level. It is known that carbohydrates are found in the human and animal organism in the form of glucose (transportable form) and glycogen (depositable form). Both of these carbohydrate forms transfer easily from one to the other. The processes for regulating carbohydrate metabolism can be evaluated on the basis of changes in the blood sugar level. G. Drishel' [33] considers carbohydrate regulation as a multiloop system (Figure 32). The liver possesses homeostatic /109 mechanisms which make it possible to increase the admission of sugar into the blood when its content is low, and conversely. The pancreas also can regulate the formation of insulin by itself, without signals from the hypophysis, depending on the blood sugar level. The presence of a second hormone, glucagon, in the pancreas, whose action is opposite that of insulin, confirms the presence of self-regulation in this organ. Finally, the third, or diencephalohypophysial level is able to change the blood sugar level in accordance with the controlling actions directly by means of hormones as well as via the pancreas. G. Drishel's more detailed diagram (Figure 33) indicates that seven hormones which cause an increase in the blood sugar content oppose one hormone which lowers the blood sugar level (insulin). This may be considered as one of the mechanisms for ensuring the functional reliability of the organism since it easily /110
withstands a temporary increase in the sugar level and even reacts to a comatose condition with an extremely brief lowering of this level. The diagram indicates

the disturbing influences, which can be increased sugar absorption in the intestines, intense muscular activity, or intravenous injection of glucose. The controlling actions are signals transmitted by the central nervous system through the "master control panel", i.e., the hypophysis. Changes in the adjustment of the master panel when signals arrive from the cerebral cortex are explained by the changes in the blood sugar level during emotional stress and hypnotic suggestion.

There also are other diagrams of blood sugar level regulation. A paper was read by V. Boli at the Third International Conference on Medical /111 Electronics (London, 1960) which dealt with a method for depicting glucose homeostasis by using

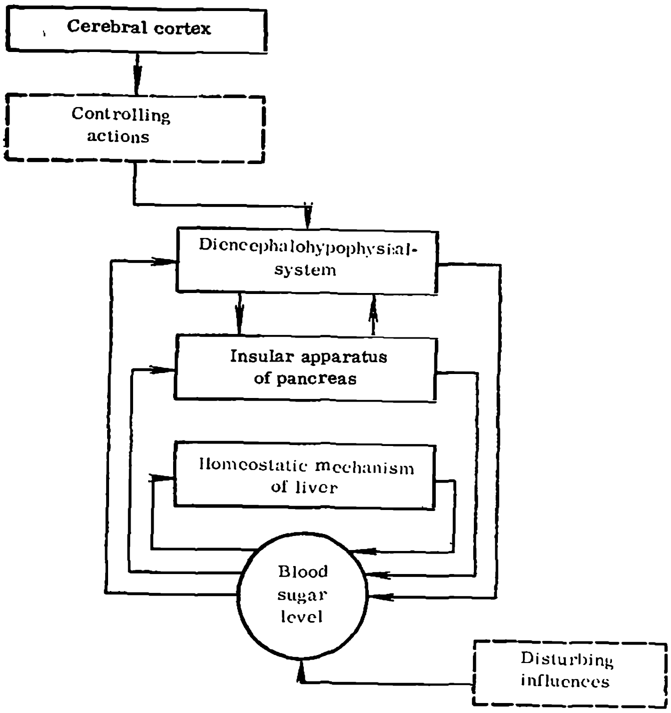
Cerebral cortex
Controlling actions
Diencephalohypophysial-system
Insular apparatus of pancreas
Homeostatic mechanism of liver
Blood sugar level
Disturbing influences

Figure 32. General Diagram of Regulation of Carbohydrate Metabolism [G. Drishel'].

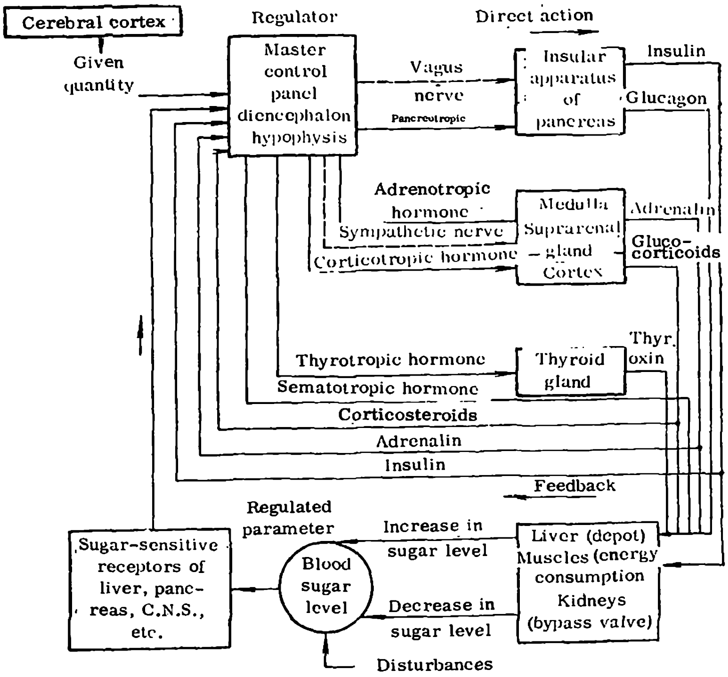

Figure 33. Detailed Diagram of Carbohydrate Metabolism Regulation [G. Drishel'].

differential levels [42]. An analog computer model was worked out for determining stability towards glucose and insulin. To do this, 17 different indices were fed into the computer. These indices characterized the glucose and insulin concentration in the blood, the rate of insulin secretion by the pancreas, the volume of blood, etc. Similar models will make it possible to improve diagnostics and to gain a better understanding of the mechanisms of biological regulation.

S. Goldman's diagram of the regulation of glucose concentration in the blood is of much interest [43]. In this author's opinion, the homeostasis of biological systems is based on three types of regulation: deviation, derivative, and integral. Figure 34 illustrates a diagram with six information channels that originate from the block which represents the glucose concentration in the blood. It is considered that the amount of glucose concentration is a stationary quantity. An increase or decrease in concentration is transmitted /112 through the (+) ΔC and (—) ΔC channels. Each of these channels may be connected to a specific organ. When the concentration drops, information is transmitted through the d/c/dt (—) channel to the cortical layer of the suprarenal glands, which then secretes the adrenalin that is transported to the liver. The liver, in turn, converts the glycogen reserves into glucose, which is secreted into the blood. The d/c/dt (+) information may go to the pancreas to stimulate

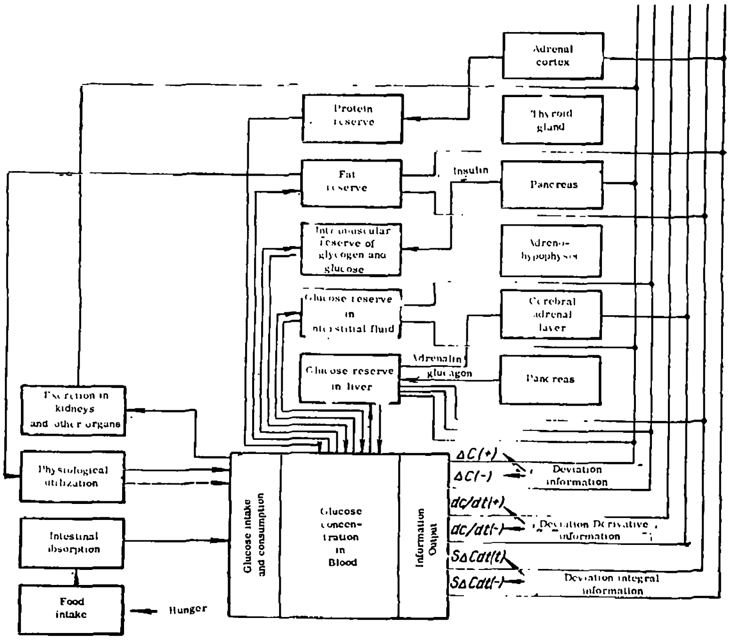

Figure 34. Diagram of Glucose Metabolism Regulation [S. Goldman].

insulin secretion. S. Goldman further states that the error integral information ∫ΔCdt(+) and ∫ΔCdt(—) goes to the organs in which the fat reserves are stored, whereby the first probably stimulates fat formation and the second mobilizes it.

Burn Shock as an Automatic Regulation Process

Many attempts have been made to employ cybernetic concepts in the analysis of pathological processes and various syndromes.

N. M. Amosov writes about "disease programs", bearing in mind the rearrangement of the activity of all the organism's systems on new levels. This is caused by the action of various injurious factors [8]. P. Cheyshvili considers a disease syndrome and the state of narcosis from the standpoint of cybernetics [44]. P. K. Anokhin describes the cybernetic mechanism of thirst [45]. The cybernetic analysis of acute conditions is of much interest; e.g., shock, collapse, coma. The construction of mathematical models of these conditions would make it possible not only to quickly diagnose them with regard to their degree of severity, but also to foretell their course and to select the most optimum methods of treatment. The complexity of studying the interaction of the various parameters of an organism's systems during pathological processes can be demonstrated in an example of burn shock, the cybernetic study of which was performed by Ye. V. Gubler at the S. M. Kirov Order of Lenin Military-Medical Academy. In his opinion, the main purpose of regulation in pathological processes is to prevent any of the physiological parameters from going beyond the limits compatible with life and to prevent deviations from the norm on the part of a number of other parameters. Thus, as a result of a transient process, a new stationary state (chronic disease) or transient catenary process may arise in a complex system of regulation directed toward self-preservation, which ultimately leads to normalization of the system or to death. /114

Ye. V. Gubler devised a diagram of the mutual influences of various functional units in burn shock with an indication of the direction of these influences and their sign. It is essentially a diagram of regulation loops incorporated into a transient catenary process. The solid arrows in Figure 35 indicate the influences which cause deviations of physiological parameters from the norm. The dotted arrows denote the regulating influences. The circles are centers of the regulation loops. Although the details of the diagram are not based entirely on known data (certain interrelationships had to be surmised), the diagram's value with respect to systemizing existing knowledge, and especially as a preparatory stage for the mathematical simulation of shock, arouses no doubts.

A detailed explanation of Ye. V. Gubler's diagram goes beyond the scope of this section, the purpose of which is to illustrate the possibility of cybernetic analysis of even such a complex state of the organism as burn shock. An examination of all the interrelationships in this diagram is contained in Ye. V. Gubler's article, "Burn shock as an automatic regulation process"[46]. A burn is a "disturbing" action which withdraws a complex biocybernetic system from a stationary state and causes transient processes on all levels of regulation. It is not yet possible at the present time to simulate the entire process of burn shock, but the creation of models of individual aspects of it (such as

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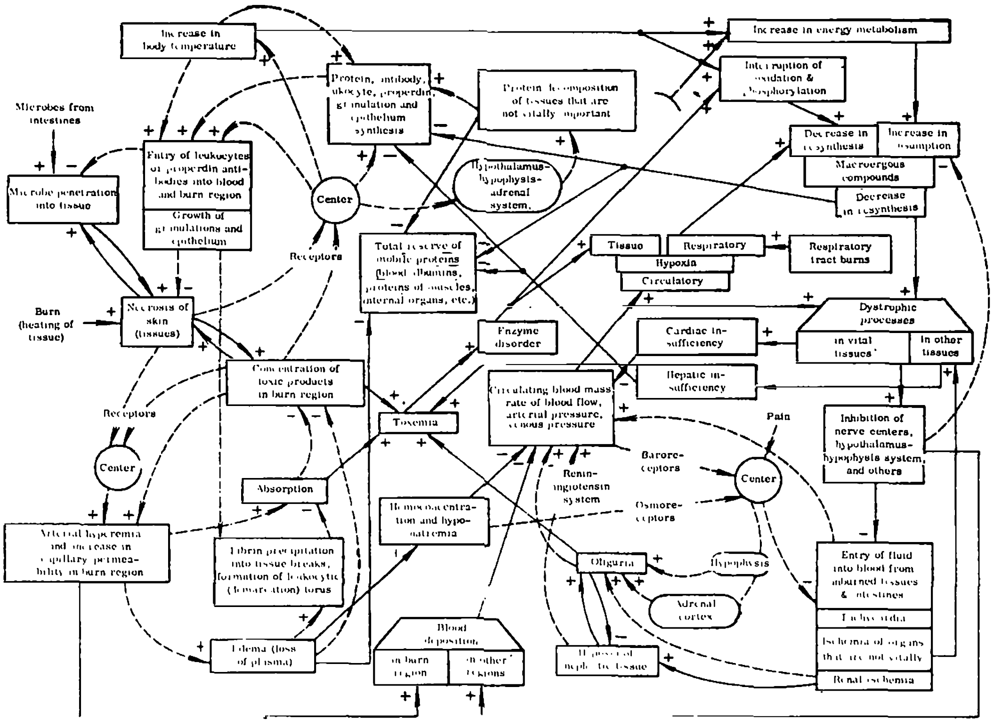
Increase in body temperature
Increase in energy metabolism
Interruption of oxidation & phosphorylation
Microbes from intestines
Protein, antibody, leukocyte, properdin, granulation and epithelium synthesis
Protein decomposition of tissues that are not vitally important
Decrease in resynthesis
Increase in consumption
Macroergous compounds
Decrease in resynthesis
Entry of leukocytes or properdin antibodies into blood and burn region
Growth of granulations and epithelium
Microbe penetration into tissue
Center
Hypothalamus-hypophysis-adrenal system,
Receptors
Total reserve of mobile proteins (blood albumins, proteins of muscles, internal organs, etc.)
Tissue
Respiratory
Hypoxia
Circulatory
Respiratory tract burns
Burn (heating of tissue)
Necrosis of skin (tissues)
Dystrophic processes
in vital tissues
In other tissues
Enzyme disorder
Cardiac insufficiency
Concentration of toxic products in burn region
Hepatic insufficiency
Circulating blood mass rate of blood flow, arterial pressure, venous pressure
Receptors
Toxemia
Pain
Inhibition of nerve centers, hypothalamus-hypophysis system, and others
Center
Baroreceptors
Renin-angiotensin system
Center
Absorption
Osmoreceptors
Hemoconcentration and hyponatremia
Arterial hyperemia and increase in capillary permeability in burn region
Fibrin precipitation into tissue breaks, formation of leukocytic (demarcation) torus
Oliguria
Hypophysis
Entry of fluid into blood from unburned tissues & intestines
Adrenal cortex
Tachycardia
Edema (loss of plasma)
Blood deposition
in burn region
in other regions
Ischemia of organs that are not vitally
Renal ischemia
+
−

Figure 35. Diagram of Interrelationships (Regulation Loops) in Burn Shock. Rectangles Represent Physiological Parameters that go beyond the Norm.

changes in fluid-electrolyte balance, oxygen balance, or hemodynamics) is quite realistic. Such models will aid us to more rapidly acquire precise knowledge on the pathogenesis of burn shock, will make it possible to understand the peculiarities of a number of other acute conditions, and will be of practical use in shock diagnostics and treatment.

Neurocybernetics

The problem of studying the mechanisms of the human and animal brain continues to remain one of the most complex and interesting problems in biology. Its importance is increasing in connection with the progress of science, its biological divisions as well as its technical ones.

Among the numerous "secrets" of nature which modern science is attempting to decipher, the greatest secret, perhaps, is the brain. What is the basis of thinking? How are expedient reactions of living organisms to the external /115 medium for preserving and maintaining life generated? What are the intimate mechanisms of fine control of the work of organs and systems and the principles of organization of an entire living organism? All of these questions and many others similar to them, which are directly related to cerebral activity, are of tremendous interest to physicians, physiologists, psychologists, philosophers, and other specialists that constantly encounter the problems of interrelationship between the living and the nonliving, the psychic and the somatic, the conscious and the unconscious, and the simple and the complex, in their practical and scientific work. Since ancient times, scientific materialists have sought scientifically based answers to these questions. Beginning with the middle of the last century, science has approached the investigation of cerebral activity as the main control center in living organisms. I. M. Sechenov's book, Cerebral Reflexes, was the first to consider the brain as a complex system. The genius of I. P. Pavlov pointed out to science new ways of objectively studying the work of the brain. The purposeful investigations of I. P. Pavlov and his numerous students and followers created an ordered structure for studying higher nervous activity.

Modern science has accumulated a huge amount of facts and has established a number of laws that characterize many aspects of the activity of the central nervous system, the cerebral cortex in particular. However, in spite of the significant success in explaining the mechanism of certain elements of this activity, (neuron activity, conditioned reflex, central regulation of autonomic functions), the general laws that characterize the functioning of the brain as a thinking organ, as a command post which determines the behavior of the organism, or as a center that unites the individual parts into a single organism, remain insufficiently known. It has become evident that the brain is a very complex system whose investigation requires all the knowledge acquired by mankind. In connection with the emergence and development of cybernetics, i.e., the science which investigates the principles of functioning for systems of enormous complexity, new possibilities arose for investigating the brain, penetrating its secrets on the basis of contemporary mathematical and physical concepts. The central nervous system was the object of the first cybernetic investigations, and neurophysiology essentially should be rightfully considered as one of the forerunners of cybernetics. As N. Wiener indicated, the neurophysiological research that he performed in collaboration with A. Rosenblueth played an important role in establishing opinions which soon led him to the formulation of cybernetic concepts. Questions related to the functioning of nerve mechanisms /116 have occupied first place with regard to the depth and volume of research in cybernetics in the years since that time. There are practically no current problems in the field of neuropathology and psychiatry, neurophysiology and psychology, where a cybernetic interpretation has not been attempted. The genesis of epileptic seizures and memory mechanisms, the activity of the nerve network and the neuronal function, the conditioned reflex and recoding of afferent information have all become subjects of cybernetic study. Today we can already speak of the emergence of neurocybernetics as an independent field. Neurocybernetics is the science concerned with the transmission, storage, and processing of information in the human and animal nervous system.

We define neurocybernetics as the entire complex of questions prompted by a consideration of the nervous system, at all of its levels, as a cybernetic system. In this sense the definition of neurocybernetics given by S. N. Braynes, A. V. Napalkov, and V. B. Svechinskiy [47] is narrowed. In their opinion, "the object of neurocybernetics is to study the laws of circulation and processing of information in the organism -- environment system". If the nervous system is considered as a higher control level in the organism, its work should necessarily be composed of mechanisms that balance the organism with both the external and internal medium. Balancing with the external medium is possible only on the basis of constantly considering the state of the internal medium since this balancing also is the purpose of homeostasis.

The human and animal nervous system, and especially the brain, is undoubtedly the most complex cybernetic system known on Earth. Its comprehension requires the simultaneous use of many methods. The study of the mechanisms of the entire brain is based on the creation of certain hypotheses and their validation by means of various experiments. This approach, for example, is the basis of contemporary conditioned reflex theory. A different approach became possible quite recently in connection with the advances made in the area of molecular and cellular biology, and with research on the volume of information on these lower levels. The construction of neuron models, the study of nerve networks, and the analysis of protein synthesis mechanisms led to the creation of stable concepts concerning the functional structure of a number of lower levels of organization of the nervous system. These concepts were the new foundation for studying the brain, since the formation of higher levels is based on the use of a number of laws of the lower levels. At the same time, new laws arise with a /117 transition to a higher level. It may be stated in a general sense that specificity increases at each higher level. The thought that there exists such a level (submolecular, electron, etc.) at which biological laws preserve their specific character only with respect to nonliving matter and do not differ from one another for the most diverse forms of objects, tissues, organs, and systems is theoretically quite valid. Thus, the brain along with the biological higher-order specificity also possesses elementary specific mechanisms which relate it to any other element of a biological system.

Neurocybernetics, consequently, studies certain informational features of the nervous system which make up the specific nature of only the given, higher level of control in a living organism, but depends upon already studied laws inherent to lower levels, as necessarily participating in the creation of this new specific. From a philosophical point of view, the object of investigating neurocybernetics is the problem of transposing quantitative changes into qualitative ones on one of the stages of evolution associated with formation of such an organizational level; one that unites the regulation of the organism's internal medium with its balance concerning external disturbances. In other words, neurocybernetics intends to give an answer to the following question: does anything new occur in the information exchange mechanisms as a result of the appearance of the nervous system and its higher division, the cerebral cortex?

Most of the brain's work consists in converting the information that it receives by way of numerous channels from various receptors. The brain, in turn, continuously sends information to the periphery in the form of commands which correct the activity of various systems of the organism and ensure an adequate reaction to the action of external factors. The brain is also the greatest store of information.

All the indicated properties of the brain have analogies in modern computers, automatic regulation systems, and servomechanisms. But it would be incorrect to consider that these analogies can provide an exhaustive answer to questions referring to the general principles of brain activity. First of all, many functions are accomplished "exclusively" by the brain, i.e., they have no analogy in engineering. Some of these functions, such as the ability to recognize a specific type of information, for example, are being recreated with success by engineers at the present time (see the chapter, "Bionics"), while others, consciousness and creativity, for example, cannot be recreated artificially. Secondly, the brain's activity is affected by factors which have absolutely no /118 significance for engineering devices. We are bearing in mind the emotions and general condition of the organism (e.g., the tonus of the cortex, which is regulated by impulses from the subcortex, from the reticular formation to be more exact). There are data on the fact that the reticular formation also selects the signals that proceed to the brain on the principle of their relative newness. An unusual stimulus increases the tonus of the cerebral cortex. Insignificant stimuli bring about an inhibitory condition. The reticular formation, thus, is a unique preselector.

The brain is a system of extraordinary complexity, and such systems are characterized, as we know, by qualitatively new properties and peculiarities that are not observed in the elements from which these systems are composed. Thus, for example, knowledge of the principles of operation of an electron tube, flip-flop counter, and logic circuits does not yet provide an idea of the setup of an electronic digital computer. What, for example, could a detailed study of cross sections of a modern television set provide towards a judgement concerning its operating principles? An analogous situation is observed in the study of data on the cyto-architecture of the brain.

In the investigation of cerebral activity we come in contact with the most diverse functional systems: from extremely simple ones (neuron, unconditioned reactions) to very complex ones (consciousness, thinking). The task of synthesizing an entire system from elements arises. This synthesis is possible only by applying mathematical methods to biology. The mathematization of biology is an extremely important characteristic of cybernetics and provides it with a certain "universality", since the same mathematical expressions can describe various processes in biology and engineering.

The application of mathematical logic, probability theory, and the theory of games to the study of the brain has made it possible to establish many new principles that conceptualize cerebral functioning as a complex system. Simulation is an important method of neurocybernetics. By simulating individual functions of the brain, we can practically verify certain propositions concerning its internal structure, and simultaneously advance new hypotheses on the basis of studying the model's behavior. No less important to neurocybernetics is the "black box" method. The brain is a very large and complicated "black box". It has a large number of inputs and outputs (receptors and effectors) which interact with one another and vary their characteristics under the action of external factors. We can establish definite laws for the functioning of a complex /119 system by acting on its input circuits and observing its behavior.

I. P. Pavlov extensively used the "black box" method. He studied the reactions of a complete organism to various stimulants and, by comparing the input signals with behavioral information of the animals, he constructed various hypotheses concerning the mechanisms of activity of the cerebral cortex. I. P. Pavlov set up new experiments and simulated his discovered solution to check his hypotheses.

Along with the "black box" and simulation methods, the search for algorithms for information processing in the brain is of definite value. Special experiments with humans and animals are performed to work out algorithms. The algorithm determines which signals are to be stored, which are to induce a motor reaction, and what ratios of new and presently available information are necessary at the various operating levels. A function can be simulated on the basis of a known algorithm, whereupon the actual sequence of actions is observed.

One of the essential features of the brain is its ability to form new modes of behavior and to create new algorithms and programs of activity. Systems that provide for independent programming of their work in accordance with the goal set before them are said to be self-organizing. The brain is the most sophisticated self-organizing system. The brain integrates all aspects of the organism's activity by means of conditioned reflex mechanisms, e.g., autonomic, behavioral, and psychic activity. In the opinion of A. A. Krauklis [48], there exists self-regulation of higher nervous activity which ensures constant adaptation of the brain to the dynamic situation of the external and internal medium. The principle of self-regulation of higher nervous activity consists of conditioned reflex monitoring of the information that enters the brain (afferent), the information that is slowed down in the brain, and the information that leaves the brain (efferent). Krauklis establishes three types of self-regulation directed toward the optimization of intracentral nervous activity. The first type of self-regulation consists of amplifying or weakening the outgoing pulsation, which leads to a change in intensity of the effector reactions. The second type of self-regulation is defined as the ordering of afferent influx states. This arrangement is accomplished, on the one hand, by the appropriate ordering of intracentral inhibitions that act on the selective behavior of afferent signals, and by the ordering of afferent activity states, on the other hand, which determines reverse afferentation. The third type of self-regulation /120 is associated with conditioned reflex influences, including intellectual-emotional motivations and vocal reactions. All three types of self-regulation are interrelated, interdependent, and socially directed. Krauklis gives the following definition: "The state of higher nervous activity (i.e., the relationship per unit time between the incoming, circulating, and outgoing pulsation, and the interrelationship between the facilitating, inhibitory, and dominant systems of neural connections) should be considered to be optimum if an adequate (depending on the situation; e.g., socially adequate for man) level of integration of nervous activity is ensured when the brain exhibits economic energy consumption and possesses functional reserves, i.e., a level at which the brain reflects the conditions of the external medium".

Being a complex self-organizing system, the brain possesses the ability to form new modes of behavior. This ability is exhibited in elementary form in the generation of conditioned reflexes in animals. The conditioned reflex is the realization of the principle of ultrastability, which consists in the active search for a stable state. As the result of some influence, a reaction occurs that is directed toward maintaining the system's stable state. Thus, if an animal effects a conditioned defensive reflex to sound, the drawing back of its paw is nothing more than a goal-directed reaction. Contradistinct to such "conscious" actions of a self-organizing system, a large category of reactions exists known as unconditioned reactions. Unconditioned reactions are the actions of a complex system based on a pre-compiled rigid program. Here, in response to a certain influence, a single-value response is obtained. In engineering we find an analogy to this process in numerous danger signalizers, e.g., photoelectronic systems with increased sensitivity in the infrared region of the spectrum, including sirens that are actuated in the event of fire in the observation zone. Modern automatic assembly lines in machine construction, which accomplish the complete manufacturing cycle from the preparatory operations to packing of finished parts, are also designed on the principle of the conditioned reflex. They are automata with a strict operational program and accomplish a complex chain of unconditioned reactions. The activity of the internal organs of the nervous system is also regulated according to the principle of unconditioned reflexes. Certain important influences or changes in the organism's internal medium cause certain shifts in the state of various internal organs. Thus, the action of a painful stimulant causes an increase in blood pressure, an increase in pulse rate, an increase in sugar content in the blood, etc. Cybernetic research on systems with rigid programs imposes a number of problems /121 whose solution is possible only with a complex bioengineering approach. Some of these problems include: the realization of given complex modes of behavior of a system in a series or sum of diverse actions, the inclusion of operational programs depending upon the type of action, etc.

The study of the principles of information processing in the brain is an extremely important prerequisite for the subsequent study of the more complex forms of its behavior. I. P. Pavlov's work is of tremendous value in this area. Let us first of all mention certain general questions on cerebral functioning. Many stimuli come from the external medium. The usefulness of one signal or another, however, is not known in advance. The brain selects the useful signals on the basis of time coincidence of a new signal with one already known (the conditioned inhibition principle). The greater the number of coincidences in this case, the stronger the reaction, and the more accurate the identification of the stimulant. The organizational expediency of living systems is expressed here, since a single coincidence of two signals may actually be a unified, random coincidence. Multiple coincidences are more reliable. Thus, the brain is protected from false information. In the formation of complex behavioral reactions, simple conditioned reflexes are united into complex functional systems. The concept of the systemic nature of cerebro-cortical functioning is one of the important outcomes of Pavlov's study. S. N. Braynes et al. [47] indicated the possibility of an algorithmic description of complex systems of conditioned reflexes in animals, and also the simulation of behavioral reactions by means of nerve networks.

A particular form of reaction to stimulants developed during the process of active adaptation to infinite changes in the external medium of living organisms. It is known as the orienting reaction. This reaction originated at the earliest stages of evolution and is inherent to even the most elementary organized representatives of the living world. The orienting reaction is a means of active extraction of information necessary to a living organism for the timely anticipation of probable injurious actions. G. I. Polyakov [49] writes: "An animal is not a system which, similar to a plant, passively 'experiences' an external flow of influences. In the sphere of animal life similar actions enter the system that are already expected, i.e., it is previously adjusted to the probability that some unpredicted events can occur in its surrounding /122 world (a predator in the process of hunting, for example, acts on the principle of this 'anticipating circuit'). The orienting reaction is an expression of the organism's adjustment to the uncertainty of possible changes in the environment, thus insuring it from the accident of being caught off guard. In this respect the animal may be equated to a system that anticipates events".

Ye. N. Sokolov [50] devoted a special article to a consideration of the orienting reflex as a cybernetic system. According to Sokolov's concepts, the orienting reflex is stimulated by mismatch impulses that occur when the afferent stimulant does not coincide with the neural model of the stimulus. This model is prompted by memory mechanisms and forms extrapolative impulses of the future value of the stimulus. If the actual and predicted stimuli coincide, there is no orienting reflex. Consequently, there must be a special comparator (comparing device) which generates signals that excite the effector centers of

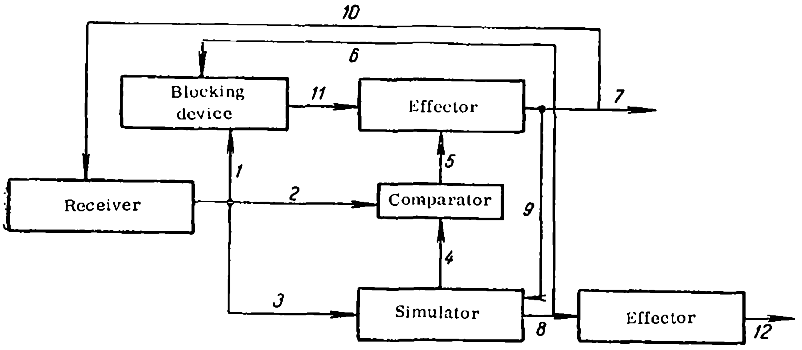

Figure 36. Structural Diagram of Orienting Reflex [Ye. N. Sokolov, 1963]. Specific Afferent Stimulation Proceeds: 1 = to Afferent Mechanisms of Orienting Reflex Through Conditioned Inhibitory System (Blocking Device); 2 = to Comparison Mechanism; 3 = to Simulator; 4 = Impulses Generated by Extrapolative Mechanism and Sent to Comparison Mechanism; 5 = Mismatch Signal that Occurs when Afferent Stimulation and Extrapolated Value of Signal do not Coincide; 6 = Extrapolative Impulses used to Block Afferent Signals; 7 = Efferent Impulses of Orienting Reflex; 8 = Extrapolative Impulses of Conditioned Reflex; 9 = Reverse Effect of Orienting Reflex on Mechanism which Forms Neural Model of Stimulus; 10 = Reverse Effect of Orienting Reflex on Receptor Apparatus; 11 = Signals to Centers of Orienting Reaction; 12 = Time-Based Effector Mechanism of Conditioned Reaction.

the orienting reflex. If the stimuli are repeated, the orienting reflex is extinguished since extrapolation is made more precise; and, finally, a conditioned reflex is formed. The orienting reflex is then inhibited, evidently by blocking the flow of afferent impulses. Figure 36 illustrates a structural diagram of an orienting reflex.

The orienting reflex is only the very first link in a complex chain of physiological phenomena directed toward the determination of the relationship of the organism to the events taking place around it. The orienting reflex occurs during the primary action of some factor on the organism. Multiple influences of the same factor cause the formation of a conditioned reflex reaction and temporary communication occurs. The progressive development of conditioned reflex activity is associated with complexity in the evolution of orienting behavior. The organism perceives information of use to it through orienting reactions. A specific relationship of the organism to a given type of information is secured as a result of closing the temporary communication. G. I. Polyakov [49] writes: "The orienting reaction generates the organism's relationship to the signalization which carries uncertain information on what is being changed and where, i.e., information only on the possiblity of the occurrence of something that may have a significant meaning. The purpose of the orienting reaction is to impose the obtained messages on the subsequent definition of biological significance". Contradistinct to this, the closed and se- /123
cured temporary communication is a reflex expression of the relationship of the organism to a source of completely certain information which signals the appearance of changes that take place with a definite regularity, which makes it possible to predict what must occur. When the conditioned reflex is closed, thus, the uncertain information is converted into certain information, i.e., the entropy of the messages sent to the brain decreases. Statistically, the probability increases in the formation of the temporary communication that the given reaction will be accomplished from among the possible ones. The organism's response during an orienting reaction is difficult to determine in advance and, consequently, the entropy of the messages is great.

One of the important features of the brain consists in the fact that its reaction depends not only on current information, but also on previous experience.

A characteristic peculiarity of the brain is its ability to selectively fix vitally important information and to actively search for this information. The finding of food leads to the fixation of data with respect to shape, color, and odor of the food, its location, and other details. On the question of a /124
material information carrier, N. Wiener expressed a proposition concerning information storage in the form of a definite structure stipulated by changes in synapse permeability [51]. The fact is that the transition of stimuli from one neuron to another is possible only across synapses with rather low conductivity. Memorization, thus, is a decrease in the conductivity of concrete synapses which predetermines the subsequent course of stimulation. There generally occurs a state of conditioned temporary communication that is ready for operation at any moment. This type of memory corresponds to the permanent memories of computers. The immediate-access memory in the brain can be accomplished as a result of the circulation of information around a closed loop inside the brain.

In considering the methods of storing information in the brain, the conclusion can be drawn that a disturbance of information circulation is impossible to detect in the form of morphological tissue changes. Therefore, in the majority of neuropsychic disorders, which are essentially cases of the disturbances of the normal course of perception, processing, or transmission of information, structural changes should not be sought. Such psychic disorders as schizophrenia, manic-depressive psychosis, and paranoia are based on congested circulation of information in the brain. Wiener points out the common bond between methods of treating these psychic disorders by sleep or shock, with the elimination of computer malfunctions by erasing previously recorded information. The main disturbances in neuropsychic disorders are analogous to: overloading an information system, feedback disturbance, and programming disorganization.

The brain not only accomplishes and coordinates various conditioned reflex reactions of the organism, but also compares the information obtained with some earlier established criteria. Depending on the results of information analysis, conditions are created either for repeating a given reaction, for extinguishing it, or for transferring to a new action. Thus, a complex chain of reflexes which are characteristic for cerebral activity can be formed. The study of the laws of formation of complex reflex systems may be extremely essential to the development of the theory of self-organizing control systems.

The very rapid generation of stable reflexes on the basis of conditioned communication between two stimuli, one of which is traumatic and accompanied by fear, indicates that the formation of complex chain reflexes depends on the /125 character of the information which the brain receives. The emotions of fear, anger, and others cause an intense secretion of hormones into the blood. It is proposed that a sharp decrease occurs in synaptic conductivity under the action of hormones, and that conditions are created for permanent fixation of each functional communication that appears. Second and third order reflexes are easily formed on the basis of this very strong conditioned communication. This is especially expressed in humans with unstable psyches (and in certain mental disorders) when new emotions which lead to new secretion of hormones into the blood arise on the basis of the stable conditioned reflex that is formed and conditioned by the emotion. A unique "vicious circle" is thus created.

Questions concerning the functioning of cerebral mechanisms have been investigated recently on the cellular and subcellular levels. Most of the supporters are standing by the chemical theories of memory. One of the popular theories, Hyden's theory, treats memory as the process of altering the RNA structure under the action of a series of neural impulses. RNA alteration reproduces corresponding proteins, which prompts the recollection process. Contradistinct to the genetic memory, where the information is stored in DNA, the cerebral memory mechanisms are associated with RNA.

Memory mechanisms, as they are treated in association with the chemical theory, are based on the interaction of electrical processes with the RNA structure [52]. The impulses generated in the sensory or motor cells of the brain cause changes in the system of electrical circuits. The modulated repetition frequency of electrical discharges which enter a given cell disturbs the ion balance inside the cell, as a result of which the stability of the RNA bases is also disturbed. This is the transient, unstable memorization phase. RNA instability leads to the replacement of one base by another, more stable one for the given frequency from the reserve of the free bases which are always present inside the cell. Another encoding system from the RNA arises as a result and, consequently, the synthesis of another protein that is different from the previous one begins. Both the RNA and the protein, synthesized with participation of the RNA, are stable traces of memorization. A new protein may react to the same frequency of electrical signals, i.e., impulses, which earlier determined the modification; the RNA is restored, and the brain "remembers".

The hypothesis concerning the intracellular coding of information has recently been subjected to serious criticism. One of the most important positions of Hyden's theory concerning the fact that an increase in protein synthesis in /126 an active neuron is also characteristic for this coding, as is the generation and behavioral function, turned out to be inaccurate. When a physiological function is increased in any differentiated cell, protein synthesis increases since it is the universal mechanism of the interaction between the function and the cell's genetic apparatus [26]. Several facts concerning the breakdown of memory processes, and the difficulty of forming new conditioned reflexes after injecting an animal with nucleic acid-synthesis inhibitors have been interpreted to the present time with respect to substantiating the role of the RNA code in the memorization process. This can be explained, however, by a decrease in the function of nerve cells as a result of a breakdown of protein synthesis [26]. A new concept of the role of nucleic acid and protein synthesis was advanced by F. Z. Meyerson. In accordance with contemporary scientific thought, he considers that the basis for the formation of conditioned reflexes and memory is the formation of new or the expansion of existing synapses between neurons by the growth of their processes. Since activation of nucleic acid and protein synthesis is the common basis of all types of growth, it is understandable that such synthesis activation in neurons should be considered to be an absolutely necessary prerequisite for the growth of their processes and for the establishment, facilitation, or reinforcement of the intraneuron junctions which are the basis for the formation of conditioned reflexes and memorization.

The intensive functioning of a definite constellation of neurons is the basis for the generation of a conditioned reflex and memorization. Since the timely and intensive realization of the interrelationship between a physiological function and the genetic apparatus is an important point in the organization of a neuron, it may be assumed that physiological hyperfunctioning, which occurs during the process of generating a conditioned reflex or memorization, activates the genetic apparatus and leads to the growth of the neurons and their processes. A primary result of this is that the functional process takes on a plastic structure and becomes a resistant and economic basis for conditioned reflexes and memory. Thus, the main proposition of the hypothesis advanced by F. Z. Meyerson consists in the fact that the realization of an intraneuron interrelationship between the function and the genetic apparatus of a cell prevents the formation or reorganization of the intraneuron synapses and the formation of a multineuron system which makes up the structural basis for reinforcing conditioned reflexes and memory.

There exist, however, other views on the mechanisms of memory and its material substratum. The glioneural theory of cerebral functioning, developed by R. Galambos, is of definite interest. In his opinion, the organism's behavior is formed as a result of the interaction of neurons with glia. Glia is considered as tissue, the function of which is to program the activity of the neurons. Glia stores information-processing programs in the same way as the storage devices of computers, and the neurons do everything with the information they receive as prescribed by the glia [53]. /127

In our consideration of memory mechanisms, we should point out the presence of two types of memories, the immediate-access memory and the permanent memory, which are both closely interrelated. It has been proposed that both types of memories make up different stages of the same memorization process. The immediate-access memory is the information that a human being retains in his mind at each given moment. The following method can be employed to determine the capacity of the immediate-access memory. The experimenter reads aloud a random set of numbers. The test subject then tries to repeat these numbers. Since there are always ten numbers and it is equiprobable that they will follow one another, each number carries 3.32 bits of information ($\log_2 10 = 3.32$). Consequently, the volume of the immediate-access memory can be estimated at approximately 20-30 bits. When whole words or concepts are to be memorized, however, the capacity of the immediate-access memory is higher, i.e., up to 80 bits. This is explained by the fact that words and concepts are optimally encoded information. The permanent memory of the brain has been analyzed by different authors. Its volume has been estimated between 10^{10} and 10^{15} bits. The minimum volume of the memory is between 10^6 and 10^7 bits. This figure is not very great if one considers that a multiplication table contains 1500 bits. Consequently, the human memory contains a minimum of 1000 objects equivalent to a multiplication table.

In conclusion, the question of brain simulation should be examined. In the opinion of W. R. Ashby, "...the creation of a system similar to the brain with definite intellectual abilities is just as attainable in principle today as the creation of a steam engine with a given power" [54]. But the creation of an "artificial brain" must be subordinate to a definite purpose, i.e., the solution of problems that are not within the capability of man. Modern computers exceed the human being in computing speed, information-search speed, and volume of immediate-access memory. The volume of the permanent memory of computers ($10^5 - 10^7$) has the tendency to quickly approach the volume of the cerebral memory. The computers of today solve many problems that have always been considered the prerogative of man: e.g., problems in the games of chess and checkers, proofs of logic theorems, and musical composition [55]. The question of whether or not a machine thinks is more philosophical than cybernetic. /128 From the standpoint of neurocybernetics, thinking as an information process can be simulated in extremely different aspects (in the future, as well as in any other aspect) with the aid of artificial systems. In the information sense, we still know very little about the operating principles of the brain and detailed physiological, psychological, and cybernetic investigations are necessary in this area. When thought, memory, and consciousness are considered in connection with human activity, they also have a social aspect which must be taken into account when answering the question: can a machine think?

I. M. Sechenov, speaking on the machine-like character of the brain, bore in mind the goal-directivity and interdependence of all elements and processes of brain activity. The concept of a reflex as an expedient act of a living organism also is of much interest to cybernetics. The creation of more sophisticated computers cannot be only an engineering problem. Neurocybernetics, as it subsequently develops, will discover newer principles which will become technical solutions thanks to bionics. But no matter what heights computer technology reaches, the "reasoning" and intellectual capacity of machines will always be considered in association with goals and tasks assigned by man. R. Cooper [56] summarizes his work, "Artificial and natural brain mechanisms", in the following way: "Considering that the development of electronic computer technology began only ten years ago, while man has been developing for millions of years, we must recognize the great achievements of computer technology. The need for rapid calculations will increase in the missile age, but will the existing computers have useful "ideas" on how to improve the fate of humanity? This will depend on man, who must ask the machine intelligent questions".

"Man-Machine" Systems

A human operator and a control object form a "man-machine" system. Examples of such systems are a dispatcher and an electric power plant, a pilot and an aircraft, a driver and an automobile, a worker and a lathe, or a typist and a typewriter. Rapid technical progress brought about the extensive automation of industry. In very complex systems, however, in which the control algorithms have a probabilistic character, man is still the main controlling factor of the system. The operator is faced with more and more complex tasks associated /129 with the increase in the accuracy of measurements and the speed of reactions, with the increase in the number of measurements per unit time, and with the necessity of monitoring the dynamic conditions of machines on a time scale that is on the very brink of human capabilities. The problem of defining the parameters of man as a link in a complex control system arises. This problem is closely related to the more general problem of constructing mixed systems, where optimum interaction between the separate components, particularly between man and machine, is ensured.

Engineering psychology emerged in the 1920's. One of its tasks was to conduct personnel-placement tests. Engineering psychology became an independent science in the last ten years. Its practical purpose is to work out principles for matching up the designs of engineering devices (especially information-display facilities and control units) with the anatomical-physiological and psychological pecularities of man. Research in engineering psychology has been carried out on a large scale in our country, as well as abroad. Cybernetics and bionics, however, also are concerned with problems of the interaction of man and engineering systems. Bionics studies the possibilities of devising new machines on the basis of analogy with living organisms. Inasmuch as this trend involves the "biologization of engineering", it simultaneously serves the purpose of optimum adaptation of engineering systems to man. Actually, if a device is created to recognize speech, by means of which an operator can control a machine, it is also one of the solutions to the problem of optimum coordination between man and machine.

Thus, engineering psychology studies the feasibility of adapting man to machine, while bionics solves the problems of adapting machine to man. In distinction from these two disciplines, cybernetics is concerned with the theoretical investigation of the information characteristics of mixed systems which are composed of an operator and a machine, and the processes of control and regulation in these systems.

Two approaches to the investigation of "man-machine" systems are possible. The first is constituted by the fact that the operator is considered as a component of the control system and the quality of this component is evaluated in accordance with machine criteria. In the second approach, man is an information-collection center, whereby his psychological characteristics take on a prime value [57]. The contact between the operator and the machine is primarily an information process. Information is transmitted from machine to man, information is received, stored, and processed, decisions are made, and instructions are given. Data communication between man and machine under contemporary conditions is limited to two afferent channels (visual and auditory) and one efferent channel (motor acts). The number of these channels may possibly be increased in the future. The possibilities of an exchange of information between man and machine with the use of some new channels are described in Chapter V, "Bionics". /130

In examining the "man-machine" problem from the cybernetic aspect, we should pay particular attention to the exchange of information between the operator and the control object. The following stages of investigation of the information processes in a "man-machine" system can be isolated: 1) the reception of information by the operator; 2) information processing; and 3) the realization of control commands (input of control information into the machine).

Information reception is the formation of a "sensory image" in the central nervous system of the operator. The reception of this image consists of recoding a concept that is adequate for the object under investigation. There then occurs a mental image which, in the opinion of L. M. Vekker [58], has the following specific features. It is objective, since it reproduces the properties and structure of the object. It is macroscopically continuous and whole, which ensures isomorphism of the mental processes to the neural processes.

Reception is the initial stage of a complex reaction which terminates with the realization of control commands. The time of this reaction has served as the object of numerous investigations.

According to contemporary concepts, the reaction time includes the delay time in the receptors, the time of afferent and efferent behavior, the time of central transmission of excitation to the motor cells, the time of conversion of nerve excitation into effector action and, finally, the information-processing time in the central nervous system. There are many types of block diagrams which consider the operator as an information system. Figure 37 illustrates Welford's diagram [59]. This diagram is very simple. The cortical part of the analysors is represented as the "perception mechanism". The complex cortical functions of collation, recoding, and decision synthesis are designated as the "translation mechanism". Finally, the "central-effector mechanism" implies the commutation of an excitation to the motor zones of the cortex, and the formation of concrete motor or other response acts.

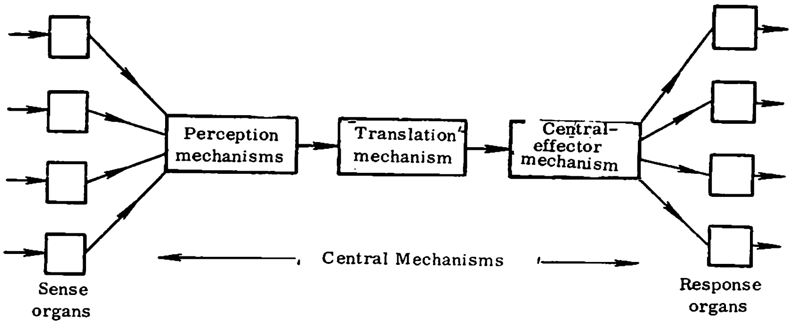

Figure 37. The Operator as an Information System [Welford's Diagram].

We can thank Professor N. A. Bernstein for most of our knowledge on the /131 physiology of the motor analysor. His monograph, On the Structure of Motions, which was published in 1947, is still considered to be a classic work [60]. Professor Bernstein is now working on a study of the motor act based on cybernetic concepts. In his opinion, every motion, regardless which kind (spontaneous or reactive), is the solution (or an attempted solution) of an action problem. But this problem, i.e., the solution of which the organism is striving to achieve, is something that should, but has not as yet occurred. Thus, an action problem is an image or model of the essential future which is encoded somehow in the nervous system [61]. The block diagram of coordination control of a motor act proposed by Bernstein includes a collation device which, together with the programming and coding units, selects the necessary solution on the basis of the goal direction of the motor act. The existence of a goal for an action which is self-directed to its accomplishment, led P. K. Anokhin to his proposition of an "action acceptor". The action acceptor is an apparatus which monitors the results of an action and compares them with the goal of the action after afferent synthesis [62]. On the basis of Bernstein's and Anokhin's theoretical concepts, Ye. I. Boyko devised a block diagram for controlling behavior with second-signal phenomona taken into account (Figure 38).

This diagram has the following components: 1) a source of mechanical energy, i.e., muscles; 2) an element that introduces given values into the system, i.e., constants, which are program elements; 3) a system of receptors for sensory synthesis of the regulated parameters (e.g., the positions of a moving /132 organ); 4) a collation device; 5) programming and coding units; and 6) motor mechanisms for coordinating and regulating the motor act [63]. Blocks 3, 4, and 5 are divided by a dotted arc into two levels. The upper level symbolizes the second signaling system and its intimate relationship with the first signaling system. The diagram shows the participation of the second signaling system in the work of the master block, the collation apparatus, and the afferent synthesis block. The interrelationship between the blocks is symbolized by the overlapping of circles on the diagram.

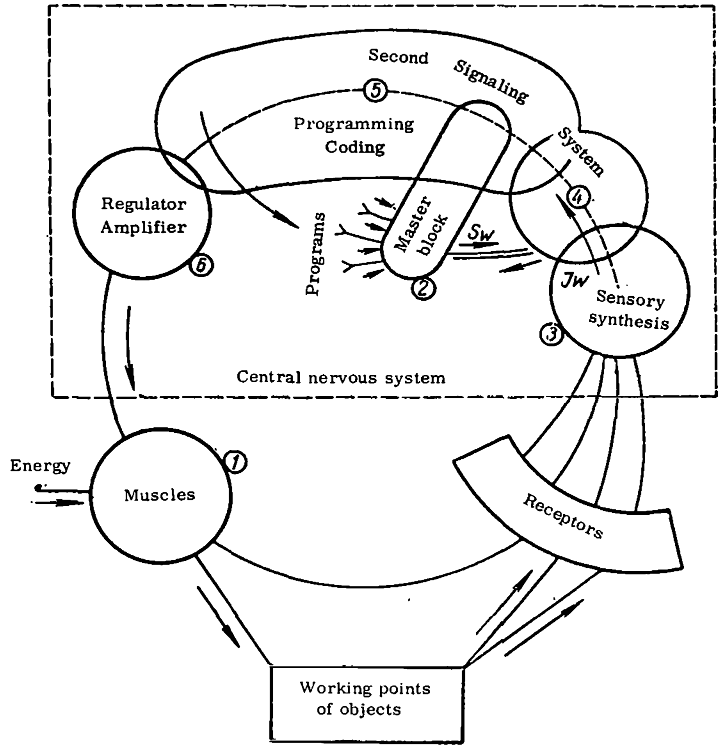

Figure 38. Block Diagram of Second-Signal Behavior Control [Ye. I. Boyko].

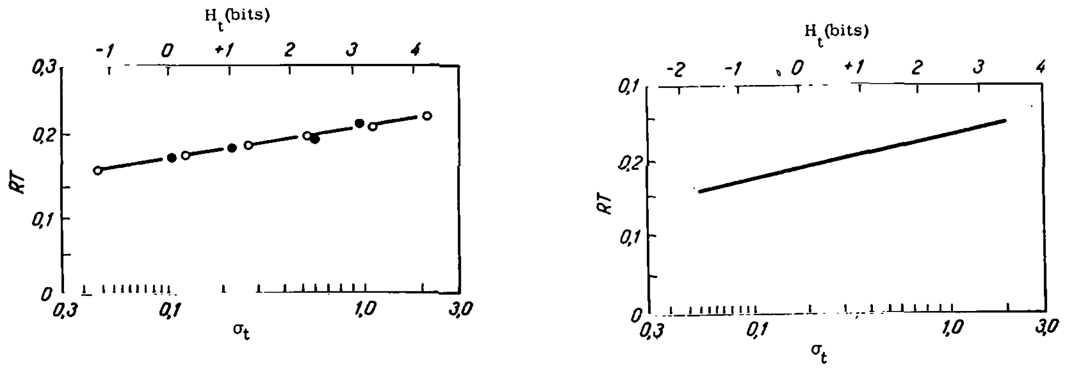

Figure 39. Simple Reaction Time as a Function of Time Incertainty of a Stimulus [E. T. Klemmer]. Left: Data from one Test Subject; Right: Cumulative Data from the Memory of Test Subjects (see text).

The motor act is the universal response of the human operator to various stimuli. The block diagram considered above indicates that the conversion of a stimulus into a motor act is accomplished as a /133 result of the interaction of various central mechanisms at the level of the subcortical centers, and the first and second signaling systems. The study of motor reaction time and its latent period pointed out that the more complex the signal, the greater the amount of time that passes from its sending to the acquisition of a response. Information theory has made it possible to quantitatively estimate the complexity of various stimuli and to explain the loss of information processing in the brain. One of the first works in this area was published by Klemmer [64], who investigated the effect of time incertainty of a signal on the duration of a simple reaction. To do this, he studied the time of a reaction to a light flash, prior to which a warning signal had been sent, i.e., an audible click. The time between the warning signal and the "starting" signal was measured from 0.5 to 5 seconds with mean square variations within the limits of one series from 0.11 to 1.82 seconds. The graph (Figure 39) illustrates Klemmer's data on reaction time as a function of the standard deviation of the time difference between /134 a warning and starting signal (σ_t). The upper graph indicates the values of the amount of information in bits (H_t), which were calculated as $\log_2\sigma_t$ minus $\log_2\sigma$, where σ is the standard deviation in a subjective evaluation of one-second intervals for the same test subject, by means of pressing a key every second. Thus, the subjective factor of the incertainty of a choice was recognized. As can be seen from the graph, there is a direct linear relationship between the reaction time and the volume of information. This question was studied in more detail by Hick, who evaluated the time of a "selection" reaction as a function of the statistical properties of a stimulus [65]. He changed the number of differentiated signals by varying the degree of selection. The reaction time could then be described by the formula $Bp = k\cdot\log_2(n + 1)$,

where n is the number of differentiated signals and k is the simple reaction time. This formula is called Hick's law. Figure 40 illustrates a graph which indicates a correspondence between Hick's experimental data and the "ideal" regularity described by his formula.

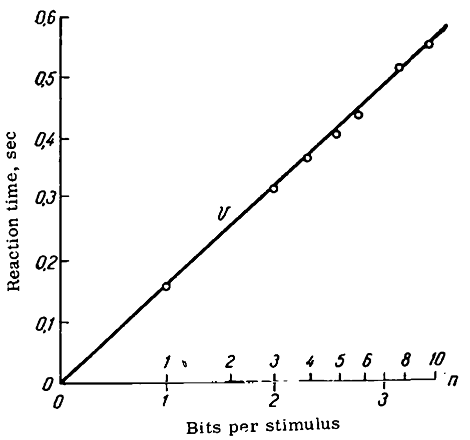

Figure 40. Hick's Data on a Selection Reaction and a Graph which Describes the Ideal Regularity of these Reactions [According to Hick's Formula].

Another investigator, Hyman [66], also varied the frequency of signal sending and introduced statistical relationships into the sequence of signals. He confirmed the presence of a practically linear dependence between reaction time and the amount of information.

In examining the questions of information processing in the brain from the standpoint of information theory, we can draw an analogy with a communication channel. The stimuli in this case (light, sound, etc.) are the information source, the sense organs are the receiver, the brain is the decoder, and the muscles are the information recipient. In this case we are dealing with the /135 transmission of information, i.e., its transmission over a communication channel. When the correct-response condition exists, the amount of transferred information corresponds to the amount of information contained in a signal. Therefore, the level of higher nervous activity or "mental" efficiency of an operator may be characterized by the amount of transferred information. The more a complex group of stimuli is subjected to analysis and the more accurate this analysis, the higher the level of higher nervous activity of the operator.

The works of A. A. Sagal [67] are of interest. Sagal discovered that the reaction time increases as the amount of differentiated attributes in the stimuli increases. In the case of conditioned reflex generation in animals, it takes 16-26 experimental days to achieve the total transfer of 0.5 bit of information per stimulus (the appearance of one out of two equiprobable signals corresponds to 1 bit per stimulus). About 1.0-1.6 bits of information per stimulus are transferred in the generation of complex chain conditioned reactions in dogs. A human transfers 5-6 bits per stimulus in 5 experimental days.

The basic characteristics of stimuli are: their statistical complexity and perception rate are expressed in bits per stimulus and in bits per stimulus per second, respectively. The possibility of calculating the amount of information contained in an individual signal has also been discussed [68]. When the statistical complexity of a stimulus is increased, the latent reaction period increases and the information processing time in the brain increases. The appearance of erroneous reactions indicates that the perception rate and the information processing rate have reached limiting values. The graph in Figure 40 illustrates Olberth's data [69] on reaction time as a function of information per stimulus. This graph ably illustrates the propositions concerning the relationship between the characteristics of a stimulus and the functional level of the cerebral cortex. As the amount of information that proceeds to an operator's input (communication channel) increases, the amount of information transmitted without errors will increase and reach a certain limiting value. The upper bound of values of the amount of information per stimulus, within the limits of which the operator can match up his reactions with the stimuli presented to him (react without errors), may be called the carrying capacity of the operator [70].

Two methods can be employed to evaluate the carrying capacity. The first method consists of increasing the rate of information admission (increasing the /136 amount of information per unit time). The second method consists of increasing the amount of information per stimulus, i.e., increasing the number of signals which the test subject must distinguish. The carrying capacity in both cases is determined by the appearance of errors. Pollak's experiments [71] indicate that subjects undergoing audio-frequency tests can differentiate no more than 6-7 tones, i.e., their carrying capacity does not exceed 2.5 bits. Garner [72] obtained exactly the same value as a result of investigating the possibilities of distinguishing between tones of the same loudness. Figure 41 illustrates the dependence between carrying capacity and the number of independent variable attributes of a stimulus for different afferent channels of a human being.

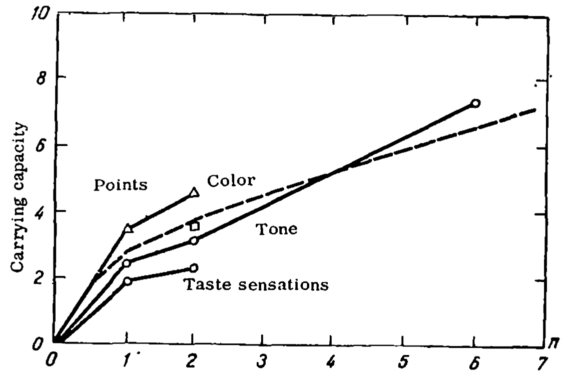

Figure 41. Carrying Capacity of a Human Operator as a Function of the Number of Independent Variables (Attributes) (n) of a Stimulus for Different Afferent Systems.

The data shown in the graph refer to subsequent experiments [70]. The estimate of the position of a point on the linear scale corresponds to the determination of carrying capacity for a case with one variable quantity (3.25 bits). For estimating the position of a point in a square (4.6 bits) we deal with two variables. An investigation of taste was conducted by giving a test subject various concentrations of salt (1.9 bits) and salt and sugar separately (2.5 bits). Sound stimuli were distinguished according to current height, amplitude, and other acoustical indices (interruption rate, spatial position, etc.). Color sensation was studied on the basis of individual colors.

The procedure for determining the carrying capacity of the visual-motor /137 system developed by A. A. Genkin, V. I. Medvedev, and M. P. Shek is of practical interest [73]. A proof table made up of eight types of symbols was proposed. The symbols are rings with breaks in different places. The break site is determined by the test subject as a number that corresponds to the position of the hour hand in the area of the ring break. Since the distribution of the rings in the table has a random character, the signals (tabular symbols) are equiprobable. The probability of the appearance of each signal is 1/8. Consequently, the average information per signal is equal to 0.5436 bits [H_{av} = Pi $\log_2$Pi + $(1 - p) \log_2 (1 - p) = \frac{1}{8} \log_2 \frac{1}{8} + \frac{7}{8} \log_2 \frac{7}{8}$].

There are 660 rings in the table. Thus, the total information capacity of the table is $H_{av} \cdot N = 0.5436 \cdot 660 = 358.8$ bits. Use of the proof table is based on the selection of one of the given types of rings. The correct selection of one given ring (useful signal) denotes the transfer of 3 bits of information (one selection out of 8 possible ones, $\log_2 = 3$). After examining the table, the test subject transfers 3 M bits of information (M is the number of useful signals). Each "useless" signal carries 0.193 bit of information since $\log_2 \frac{7}{8} = 0.193$. An error, i.e., the omission of a given signal, denotes a loss of information, which may be quantitatively estimated as $(3 - 0.193) = 2.807$ bits. If the total volume of information in the table (0.5436 N) consists of "useful" and "useless" information ($0.5436 = 3\,M + (N - M)\,0.193$), the total volume of information received will amount to $0.5436\,N - 2.807\,n$, where n is the number of errors. The carrying capacity of the visual-motor analysor is determined by the following formula:

$$S = \frac{0.5436\,N - 2.807\,n}{T}\ \text{bits/sec}$$

where T is the table-scanning time in seconds.

Questions of information processing in an operator's brain and information conversion into goal-directed responses associated with the control of certain systems are a central point in the application of cybernetics to the study of the "man-machine" problem. Information reception and motor act characteristics, to a large extent, are subjects of other disciplines: e.g., psychology, neuro- /138 physiology, biomechanics, etc. Cybernetics, however, is interested in the aspects of these problems which somehow or other affect the process of information processing. For example, optimum encoding of signals to increase the functional capabilities of an operation requires the application of cybernetic methods. It is known, for example, that the integrating instruments of aircraft navigation systems provide operational information in a generalized form and thereby increase the accuracy of control [57]. It is also known that circular scales are read more accurately than vertical scales. With regard to the motor act, coordination parameters are currently the subject of numerous investigations. Thus, one investigation [74] studied the process of tracking a target moving at a constant speed on a visual indicator. The operator sent out brightness markers whose positions were matched up with the target by manual control. There occured deviations of the markers from the target whose values are random functions of time. It was possible to create a mathematical model of these deviations which quite accurately depicted the operator's activity. The quality of manual control, in general, is related not only to the transfer of information in the central nervous system, but also to the peculiarities of the muscle system. A muscle is an element with multiple feedback [75]. A minimum of three systems participate in the regulating activity when nerve impulses are distributed from centers to muscles. The first system determines the contractile function of the muscles. It consists of motoneurons and muscles with proprioceptors embedded in them. The impulse information in this system is distributed from the cells of the anterior horns of the spine to the muscles and from their receptors in a reverse direction across the posteroradicular system to the spinal centers and again to the motoneurons. The second system adjusts the excitability of the proprioceptors to an optimum level. The third system, the axon-collateral system, is intended for self-regulation of the motoneurons. Thus, after a command is generated and sent to the effector block of a "man-machine" system, complex events associated with information exchange and processing, automatic regulation, and feedback develop on the periphery.

One of the most common forms of activity of a human operator is tracking, which can be defined in general terms as matching up two or more dots, lines, or surfaces, or, generally speaking, as the comparison and leveling of individual variable phenomona to some common level. Some of these phenomona vary independently /139 of man, while others depend on his controlling motions [76]. There is one- and multidimensional tracking, depending on the number of control objects. The activity of an operator that performs tracking can be considered from the positions of the theory of servo systems.

For the most part, man is a self-teaching system. "Self-teaching", from the cybernetic standpoint, is the optimization of a system, which is self-accomplished by means of internal adjustment and readjustment of its organization. The "human servo system", if it is characterized by technical terms, refers to oscillatory extremal systems with a self-changing (optimizing) structure and self-adjusting parameters. G. V. Sukhodol'skiy [76] has proposed a block diagram of such a system, which contains prediction and augmentation mechanisms (as correcting units), a search mechanism, integrators, and circuits which correct the value and sign of errors, and their first and second derivatives.

The augmentation mechanism provides a maximum speed of target "lock-on", which is necessary because of the inertness of the system. The prediction mechanism /140 also helps to eliminate the system's inertness. The distinction in operation of the first and second mechanisms consists in the fact that the augmentation mechanism creates a transfer function with overshoots. The prediction mechanism creates a smoother transfer function (See Figure 42).

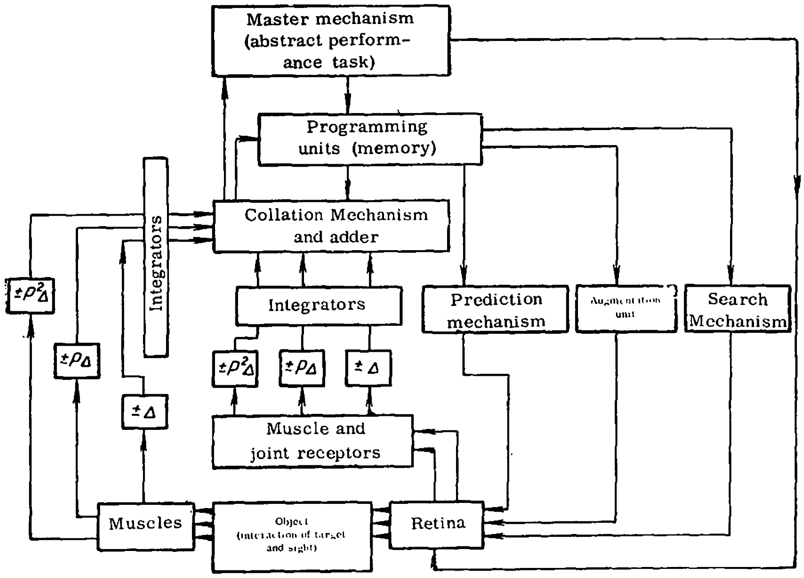
Master mechanism (abstract performance task)
Programming units (memory)
Collation Mechanism and adder
Integrators
Integrators
Prediction mechanism
Augmentation unit
Search Mechanism
±P²Δ
±PΔ
±Δ
±P²Δ
±PΔ
±Δ
Muscle and joint receptors
Muscles
Object (interaction of target and sight)
Retina

Figure 42. Block Diagram of Human Servo System [G. V. Sukhodol'skiy].

One of the most important characteristics of the "human servo system" is stability. When the target position changes, the system builds up and undamped oscillations occur in the first and second periods. The length of one period is about 0.5 second. The organization of the search process changes in the course of system optimization. The regulation time decreases, wherein an important role is played by the feedback with respect to $\pm P^2\Delta$.

The "human servo system", on the whole, is significantly more complicated than engineering servo systems and is superior to them in many respects. In view of its functional redundancy, it is sometimes less stable and accurate for performing highly specialized tasks, but more resistant and reliable.

In spite of the large number of diversified problems facing the investigators, one of the most important ones is the quantitative analysis of the process of information processing. Serious attention is being given here also to the study of the effect of extremely diverse conditions and factors on this process. These factors can be divided into three groups [57]:

-- information factors (type of problem, character of signals, time limitations, logic capabilities, etc.);

-- technical factors (coding method, type of object, means of information transmission, etc.);

-- subjective factors (individual peculiarities, state).

In conclusion, we shall discuss the last group of factors. In addition to the psychophysiological capabilities of man, which restrict his carrying capacity or control accuracy, the general condition of the organism is of importance. Disease, emotion, apprehension, pain, fatigue, and so forth essentially modify the parameters of an operator as a component of a complex system. In some cases this component alters its functioning or performs its functions with a large number of errors. It is especially difficult to monitor the appearance of operator conditions which are not accompanied by obvious deviations. These are primarily tensions. It has been proposed to monitor the emotions by means of electroencephalograms with the calculation of their autocorrelation functions, distribution laws, etc., by means of pulse rate and dispersion, by means of galvanic skin response, and so forth. The automatic manifestation of emotional states /141 which prevent the further utilization of the operator as a component in a "man-machine" system is an important applied problem of cybernetics. A device must be created which could block manual control on the basis of a set of attributes and then transfer to automatic programmed control. We can now think in only the most general terms of the principles of designing such a device, since it must operate on the basis of information obtained in the course of the operator's normal activity. This device should include a sufficiently capable computer. This is necessary in order to extract a maximum of information from a minimum of data by means of mathematical treatment. Pulse analysis, operator-emotion analysis, and program analysis, for example, are very promising possibilities.

The multi-faceted character of the interests of cybernetics is clearly seen in the example of the "man-machine" problem. The following five divisions can be isolated in this problem:

-- cybernetic analysis of stimuli and communications;

-- cybernetics of analysor systems;

-- information processing in the brain;

-- cybernetics of effector systems; and

-- optimization of operator responses.

Each of these divisions refers to a definite, more specialized problem, for example, problems of information processing in neurocybernetics, but together they provide a goal-directed study of the human operator as an active participant in a complex system.

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CHAPTER THREE. CYBERNETICS AND PROBLEMS OF DIAGNOSTICS /145

A diagnosis is a complex cognitive process, the essence of which, just as /147 of any other cognitive process, consists of objectively indicating the existing regularities in human consciousness [I. N. Osipov and P. V. Kopnin: 1]. To make a diagnosis is to reveal an objective truth.

The process of making a diagnosis consists of recognizing a whole by its parts. But the modern concept of diagnostics also includes the collection of primary information on elements (parts) which are necessary to make a diagnosis. The diagnostic process does not end with only the diagnosis: it continues until the patient recovers, since the correctness of a diagnosis can be confirmed only as a result of successful treatment with the appropriate means. We know that a diagnosis is refined in the clinic during examination and treatment, so that the diagnostic process is a dynamic and flexible process.

At the same time, the diagnostic process is nothing more than an exchange of information between the patient and the physician. Indeed, anamnestic data, the patient's complaints, and the results of objective examinations are information which is processed in the physician's brain. The diagnosis is also information, which is necessary in order to prescribe the treatment. Finally, the physician's therapeutic prescriptions are information which controls the activity of the intermediate medical personnel who carry out these prescriptions.

Thus, it can be concluded that diagnostics is a typical cybernetic process associated with the collection, transmission, storage, and processing of information.

We shall now consider the "patient-physician" cybernetic system. This system is significantly more complicated than it seems at first glance, since it includes numerous means of information collection and feedback circuits (therapeutic actions).

The "Patient-Physician" Cybernetic System

In examining the diagnostic process as a process of information exchange between the patient and the physician, and bearing in mind that the diagnosis is checked by therapeutic actions (feedback), we arrive at a new class of cybernetic "patient-physician" systems. In general form, such a system consists of the following parts (Figure 43):

-- an information source and an object of action (patient);

-- means of information collection; /148

-- a physician, who converts the information into therapeutic actions;

-- means of accomplishing therapeutic actions.

From the information source, i.e., the patient, we obtain an enormous amount of diversified signals which contain information on the organism's condition.

All of the signals are not of equal interest to the physician. The more modified the signal is as compared to the standard, which is the normal condition of the organism, the more valuable it is, and the greater the amount of information it contains. In general terms, a diagnostic process is possible only in the presence of a definite volume of information. Just as a relay does not close its contacts if the current across the winding is lower than the actuation current, the information in a "patient-physician" system cannot be circulated if the volume of information from the patient is insufficient. In each specific case the system must first be adjusted for maximum information flow. The probability of making a correct diagnosis in this case becomes maximum. Unfortunately, we do not have the necessary mathematical apparatus available today to make the appropriate calculations; however, this is the only way to transform diagnostics from an empirical science into an exact science.

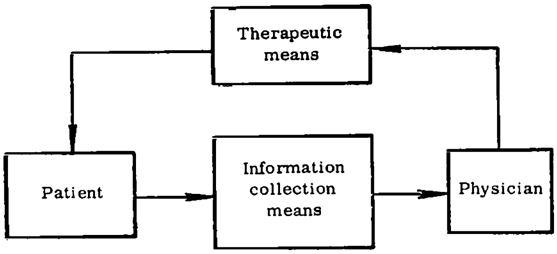


Figure 43. Diagram of Information Circulation in the Process of Making a Diagnosis.

Information is collected by various instruments and devices (electrocardiographs, x-ray machines), and also by medical personnel and by the physician himself by patient questioning, taking different measurements (height, weight), and making observations. The existing system of information collection leads to the acquisition of a great deal of data redundancy, although it does not provide for a maximum volume of diagnostic information. This happens because the clinical examination plan is not being corrected constantly. In the first /149 stages of examining a patient, this plan is essentially a feedback element in the "patient-physician" system and should be sufficiently dynamic in order to ensure acquisition of the necessary volume of information in the shortest period of time.

The information recipient, i.e., the physician, converts the information into a diagnosis. The laws which govern the formulation of a diagnosis are the object of study from all aspects of diagnostic theory. In connection with the ever increasing use of computer technology in diagnostics, interest in diagnostic theory has recently grown sharply. Questions of "machine diagnostics" will be examined in detail below. We should note here that the operations which take place in the physician's brain are extremely elementary from the standpoint of contemporary mathematics, but they are simultaneously very complicated since they contain many psychological elements which do not yield to mathematical treatment. When we speak of the physician's intuition, we mean his thinking ability for psychological analysis, as a result of which individual, insignificant symptoms are given prime importance, while the more obvious symptoms are of secondary importance. The role of intuition is great, however, only in very experienced physicians. In an overwhelming majority of cases the process of making a diagnosis can be represented in the form of a simple logical interaction between the information flow and the memory cells. The correctness and speed of making a diagnosis are directly related to the volume of information received, the volume of information contained in the physician's memory, the speed of search for the necessary memory cells, and the speed of the logic operations. This interpretation of the diagnostic process is obviously simplified, but it makes it possible to approach the analysis of extremely complex problems of diagnostic theory in association with the introduction of computer technology.

The treatment plan is outlined after the diagnosis is made. The flow of therapeutic actions is regulated according to this plan, which ultimately modifies the information structure of the information source so that it has minimum distinctions from the information structure of a healthy organism. The treatment process is accomplished in parallel with the diagnostic process. Symptomatic treatment is conducted at the stage of symptom and syndrome manifestation, and therapeutic measures which normalize the condition of separate organs and systems are prescribed in the functional diagnosis stage; finally, the result of pathogen diagnosis is the prescription of therapeutic measures for the specific pathogen involved. The correctness of the diagnosis can be evaluated on the basis of the results of treatment. Multiple measurements for checking various information characteristics of the patient are taken during treatment; the purpose of these measurements is to evaluate the effectiveness of the therapeutic measures. The faster the deviations manifested in the patient are normalized, the more accurate the diagnosis and the more correct the selection of treatment. We have especially emphasized all of these universal truths once again in order to point out the importance of a quantitative approach to the diagnostic process. If it were mathematically possible to evaluate the accuracy of a diagnosis, the effectiveness of the treatment, and the degree of deviation of the information characteristics from the norm, a means of optimizing the circulation of information in the "patient-physician" system would have been found. /150

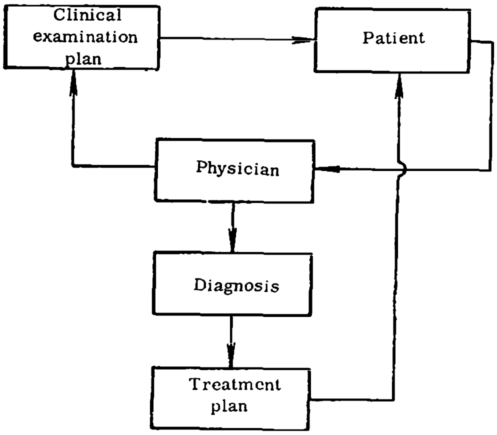


Figure 44. "Patient-Physician" Cybernetic System.

Figure 44 illustrates a block diagram of the information circulation in a "patient-physician" system. As can be seen, there are two information loops. The first loop is "patient-physician-clinical examination plan". Information on the patient is collected in accordance with the clinical examination plan. The examination begins with standard questions (what hurts?) and standard tests (temperature, pulse rate). Then, depending on the patient's complaints and the results of preliminary examination, the standard examination plan is made more specific and individualized. If, for example, the patient complains of a sharp pain in his ankle immediately after falling, and an investigation reveals swelling in this area and a sharp pain when pressure is applied, the physician concentrates all his attention on differential-diagnostic signs which are characteristic for sprained /151 ligaments, dislocation, and fracture. From the special methods of examination in this case, the physician first employs x-ray and fluoroscopy, and not electrocardiography or urinalysis, which he resorts to if the first results of examining a patient compel him to pay attention to the heart or kidneys. Thus, the clinical examination plan of each patient is also information, but it is a unique form of information, i.e., active information which controls the information source (the patient) in the sense of selecting the most important signs and indications of a morbid process in the given case. The individualized plan of clinical examination regulates the admission of information from the patient and imposes definite limits on the goal-directed search for information which is of most importance. The clinical examination plan is successively corrected during the process of sending information to the physician. In an analogy with an automatic regulation system, the role of the physician in the information collection stage consists of providing a feedback between the control object (the patient) and the control element (the clinical examination plan).

The second loop is "patient-physician-diagnosis-treatment plan". The information which ensures the therapeutic process circulates in this loop. The treatment plan is established in accordance with the diagnosis and is the information which regulates the activity of the medical personnel. The role of the physician now amounts to providing adequate treatment for a given patient on the basis of collecting information during the treatment process. This information is used to correct the preliminarily established treatment plan, as well as to introduce corrections into the continuing clinical examination plan and, if necessary, into the diagnosis.

One of the most practically important parameters of the "patient-physician" system is the information circulation time. In the first loop, this is the time from the beginning of examination to the establishment of a diagnosis and the accomplishment of the first therapeutic actions. In other words, it is the time necessary to convert the diagnostic information into control signals, i.e., therapeutic actions. The information circulation time in the second loop of this system is the treatment time. In this case, naturally, a great deal depends on the effectiveness of the existing therapeutic measures, on the form and expression of the disease, and on the individual peculiarities of the organism and other factors that are not associated with the collection and processing of information. But the treatment time in one way or another also depends /152 on the accuracy of the diagnosis, the correct selection of therapeutic measures, and the effectiveness of the control measurements made during treatment.

When we consider the information circulation time in the "patient-physician" system, we must bear in mind that it depends on the purpose of the given system. An ambulance physician must quickly render the necessary aid to save the patient's life. It is not his task to make a detailed diagnosis. The information circulation time here should be minimal. Under clinical conditions, the establishment of an accurate and detailed diagnosis takes on a prime value in a number of cases. After giving first aid in this instance, systematic and prolonged treatment must be considered. Therefore, two types of "patient-physician" systems can be distinguished: the operational system and the stationary system.

Up until now we have concerned ourselves with the operating principles of a diagnostic "patient-physician" information system in general terms. However, each of these systems has a characteristic program of information collection and processing. The rules which govern the operation of a system are called algorithms (see above). Algorithm theory is one of the elementary foundations of cybernetics. The diagnostic algorithm is the basis of the diagnostic process. Every physician performing diagnosis is governed by definite algorithms which he has learned or worked out by himself in the course of his practice. We never say that an algorithm is an orderly chain of logical deductions which leads to a diagnosis. Moreover, we usually consider that a diagnostic process is based on the intuition and inner feeling of the physician. In practically all cases, however, the entire sequence of "diagnostic" judgments, i.e., the algorithm, can be described in sufficient detail after the appropriate analysis.

The cybernetic approach to examining the process of making a diagnosis makes it possible to digress from a discussion of the specific actions of a physician with regard to a particular disease and to go on to the study of questions related to the algorithmization of the diagnostic process. The explanation and development of diagnostic algorithms will have a tremendous impact on medical science, making it possible, on the one hand, to place diagnostics in the category of the exact sciences (e.g., mathematical logic, statistics, probability theory) and, on the other hand, it will help to free the physician from numerous laborious operations involved with the collection, analysis, and processing of information, thereby accelerating and increasing the accuracy and reliability of these processes many times.

As we know, automata can be used only when the information process yields to algorithmization. Any, even the most complex, algorithm can be realized at /153
the present time by means of computer technology.

Questions on automating the process of making a diagnosis are becoming especially critical lately because the amount of data which the physician must process is constantly increasing. The number of new methods of investigation is increasing and the volume of scientific reference data which can be consulted in the process of evaluating information is expanding. Most of the qualified physicians, laboratory technicians, and other specialists at well-organized hospitals and clinics are presently engaged exclusively with the interpretation of results of various graphic and laboratory methods of investigation in the form of curves, graphs, figures, etc.

One of the important practical tasks of cybernetics is to introduce the latest achievements of engineering into medicine, particularly the automation of the processes of information collection, analysis, and processing.

A great deal is being written and said about the application of electronic computers in diagnostics at the present time. This is a very important and honorable task which requires enormous efforts from physicians and engineers. But the actual and useful application of cybernetics to diagnostics will begin, in our opinion, with simpler questions, without whose solution the effective application of electronic computers would be impossible. We are speaking of the construction of algorithms for information collection and processing, the investigation of the statistical and probability distribution of medical data, the establishment of logic bases for diagnostics, etc.

In addition to questions concerned with the algorithmization of the diagnostic process, we shall also consider the principles of construction of diagnostic information systems and the specific technical devices for realizing diagnostic algorithms.

The formulation of a diagnosis involves the performance of a number of strictly sequential logic operations. We can conditionally isolate the following three basic stages in the formulation of a diagnosis.

1. Collection of information on the patient (anamnestic data, results of physical and instrument examination, laboratory data) and information storage.

2. Analysis of collected information. Selection of the most essential data which indicate possible pathological deviations in the condition of various organs and systems.

3. Evaluation of these data by comparison with known symptoms of known diseases. Establishment of a disease, as a result of this evaluation, which most closely corresponds to the patient's symptom complex.

We shall also consider the possibilities of employing cybernetics for designing diagnostic information systems and for developing diagnostic algorithms in accordance with the indicated diagnosis-making stages. /154

Information Collection and Storage

Information collection means are an integral part of any diagnostic information system. There has been a rapid growth of information collection means in the last few years. New research methods, transducers, and instruments for examining patients and making diagnoses are being developed. This has led to an essential increase in the flow of information from the patient to the physician. The "patient-physician" communication channel can be represented as consisting of five elements:

-- an information source (patient);

-- information collection devices (transducers);

-- information conversion devices (instruments);

-- data display systems (recording devices and information storage facilities); and

-- the information recipient (physician).

By information conversion devices, in this case we also imply the means for transmitting information (telemetry, television, telephone line). A data display system could be the recording device of an electrocardiograph or an x-ray screen, as well as magnetic tape or a case history record. The ways and means of collecting medical information are diverse. The first contact between physician and patient results in information on the patient's complaints and anamnestic data represented in the form of a handwritten record. Electrocardiographic examination is accomplished by means of electrodes placed at certain points on the body surface of the test subject, an amplifier converts cardiac biopotentials into electrical signals which move the recording stylus, and the information is represented in the form of an oscillogram. The thermometer used in measuring temperature is simultaneously a device for collecting, converting, and displaying data. It is not always easy to clearly define all the elements in a "patient-physician" system. It is important to note only one exceptionally important feature of this system: the presence of an enormous number of information source outputs and only one information recipient input (the physician cannot read and listen simultaneously or accomplish palpation and write data in /155 the case history record at the same time).

Thus, a contradiction is created between the volume of information fed into the "patient-physician" communication channel and its carrying capacity. This contradiction is intensifying each year. The following methods are currently used to match the information source with the communication channel:

-- the information is fed into the communication channel in sequence (this increases the information circulation time);

-- the information is recoded in a form which is convenient for rapid perception (a special staff of physicians and laboratory technicians processes the preliminary data from examinations and analyses in this case).

-- some of the information obtained is not used (redundant information).

Questions concerned with eliminating information redundancy deserve special attention. The collection and processing of excessive information which is useless to a diagnostic process should be considered as interference in the "patient-physician" channel. Interference decreases the quality of a diagnosis and increases the information circulation time. The following question may arise: how can a physician know in advance which information is useful and which is redundant? After all, a preliminary diagnosis can be established and a more goal-directed collection of information can be organized only after collecting a definite volume of data. This reasoning is correct in principle, but the trouble is that the volume of preliminarily collected data is too great, yet is not always sufficient. This happens because information collection at the present time is considered to be an independent task apart from the interests of the diagnostic process. Information collection is not united by a single algorithm with information analysis and evaluation.

The clinical examination plan is a passive element of the system to a significant extent, and it must be corrected from the very beginning. An active information search must be organized, then the diagnostic process can be essentially accelerated, and the volume of redundant information reduced to a minimum.

It is clear that active information search requires the processing of data directly in the process of data transmission. Automatic information processing facilities are required in this case; however, effective algorithms which the physician himself can use may be devised in a number of simple cases (medical monitoring).

Another way of eliminating information redundancy on the basis of modern technology consists of optimum encoding of medical information when it is presented to the physician. /156

There are several instruments which automatically eliminate redundancy and provide information in a form that is convenient for rapid perception and evaluation of data. They include cardiotachometers for recording the pulse rate, and cerebral-biocurrent analyzers and integrators. The conventional medical thermometer is also an example of an instrument which provides the physician with only useful information. But in the case of an electrocardiogram, 8-10 values are obtained as a result of interpretation which reflect the amplitudes and time intervals of the electrocardiographic tracing, whereby an experienced specialist can easily reproduce the original tracing on the basis of these data. Consequently, an electrocardiograph collects not only useful information, but also useless, redundant information. The extraction of useful information requires a great deal of effort. It would be significantly more effective to use instruments which indicate or record only the data which is of interest to the physician; for example, instead of an electrocardiogram, the 8-10 values which the physician ultimately extracts from the electrocardiogram.

The modern recording equipment used in clinical medicine, as a rule, provides information in the form of oscillograms which possess significant redundancy and require special treatment. The recording of this information requires wideband (large frequency range) recording systems, and the number of channels must be equal to the number of parameters to be recorded.

The introduction of automatic information processing methods which eliminate redundancy will make it possible to record the necessary data in the form of a simple code: electrical signals of different amplitude or duration with a significantly lower frequency than signals of a primary character. This code may be recorded by means of recorders with extremely narrow frequency bands, and one channel may also be used to record several parameters (Figure 45). The principles upon which the formation of a conditional code is based should be selected in accordance with the level of knowledge and the research tasks. Thus, for example, an electroencephalogram can be processed on the basis of one of the following principles: determination of the amplitude-frequency composition of biocurrents, calculation of the correlation function, and determination of the phase relationships between the leads. An electrocardiogram can be processed /157 on the basis of either the isolation of one important indication (pulse rate -- cardiotachometer) or on the determination of standard time-amplitude indications, or on a determination of the frequency spectrum of the curve.

The feasibility of single-channel sychronous recording of several indices can be illustrated in an example of a system with storage devices. Figure 46 illustrates the block diagram of a 4-channel electroencephalographic device. Each of its amplifiers has an output to 4 filters with characteristics which

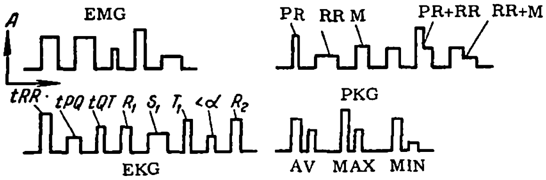


Figure 45. Methods of Encoding Certain Physiological Parameters. EMG -- Each Impulse Represents the Mean Amplitude (A) and Frequency (f) of Muscle Biopotentials in a Given Time Interval. EKG -- the Amplitude of Each Impulse Represents the Length of an Interval or Wave Amplitude; PKG -- the Power of the Signals Which Make up the First and Second Tone of the Phonocardiogram (Average, Maximum, and Minimum Value). Top Right: Recording of Pulse, Respiration, and Motion on the Basis of Recalculation into an Appropriate Code of Every 20th Respiration or Every 50th Pulse Beat, or Given Output Power of the Motion Transducer; Samples of a Recording with Signal-Code Matching are Shown.

provide for the separation of alpha, beta, gamma, and delta rhythms. The circuit has 4 integrators, one on each filter and one more for integrating the total signal. A single-channel curve is formed by means of storage elements on capacitors which, being simultaneously connected to the integrators, "memorize" the signal levels which correspond to integral biocurrent values. After "memorization", the storage-integrators are automatically "cleared" to zero, and the storage process is repeated. The information contained in the storage elements is recorded by means of a commutator on one channel in the form of a series of rectangular impulses. The curve contains a total of 20 impulses at the four electroencephalogram leads. Figure 47 illustrates a sample of biocurrent recording by means of the described electroencephalographic device. This principle can be used essentially for single-channel recording of other physiological parameters and will obviously be /159 used quite extensively in medical instrument design.

The principle of single-channel medical data recording in general form stipulates the necessity of coordinating the volume of information from the patient with the carrying capacity of the physician's analysors which receive the information. Multichannel recording devices are not suitable for the solution of practical medical problems. For example, the results of investigations conducted with the aid of a 16-channel electroencephalograph require extremely tedious and prolonged analysis and are ultimately represented to the attending physician in the form of two or three figures which indicate the power ratio of individual rhythms in certain portions of the cortex or certain generalized statistical indices of the electroencephalogram.

The problem of displaying medical information has an important value. A great deal has been published with respect to the arrangement of control panels, where questions of information display are of prime importance. But engineering psychology, which is concerned with the "man-machine" problem, considers the representatives of all professions except medicine. The problem of displaying information for a physician is just as important as it is for the operator of a radar station. Skillful organization of medical information flows and successful presentation to the physician will make it possible to sharply improve the quality and speed of diagnostics.

Special attention has recently been given to the automation of medical monitoring in surgery. Various types of monitoring and diagnostic radioelectronic equipment are used extensively in the process of complex surgical interventions on vitally important organs, primarily on the heart, major vessels, and the brain. However, in spite of the availability of contemporary operational models of this equipment, the surgeon is not able to continuously receive, systematize, and analyze the large quantity of information sent to him and to quickly determine the condition of the most important physiological systems of the organism in the process of an operation. It has been proposed to devise special radioelectronic information-recording and monitoring complexes which would make it possible to utilize the possibilities of mathematical analysis, to automatically detect deviations in physiological functions, evaluate these deviations, and provide generalized information. Visual data display will play an important part in the creation of similar devices. A special information display unit will be installed in operational models. Slowly changing parameters (pulse rate, body temperature, etc.) are illuminated by /160 figures, while rapidly changing processes are depicted on corresponding oscilloscopes. The display unit also includes a visual warning device which is actuated when a parameter transgresses the established norms, which are set up on the control panel before the operations. It is important to note that in addition to visual display and graphic recording of parameters, these devices can acquire all data in the form of punched cards which will be subsequently fed into electronic digital computers and in the form of magnetic tape which makes it possible to reproduce an entire picture of an operation when desired.

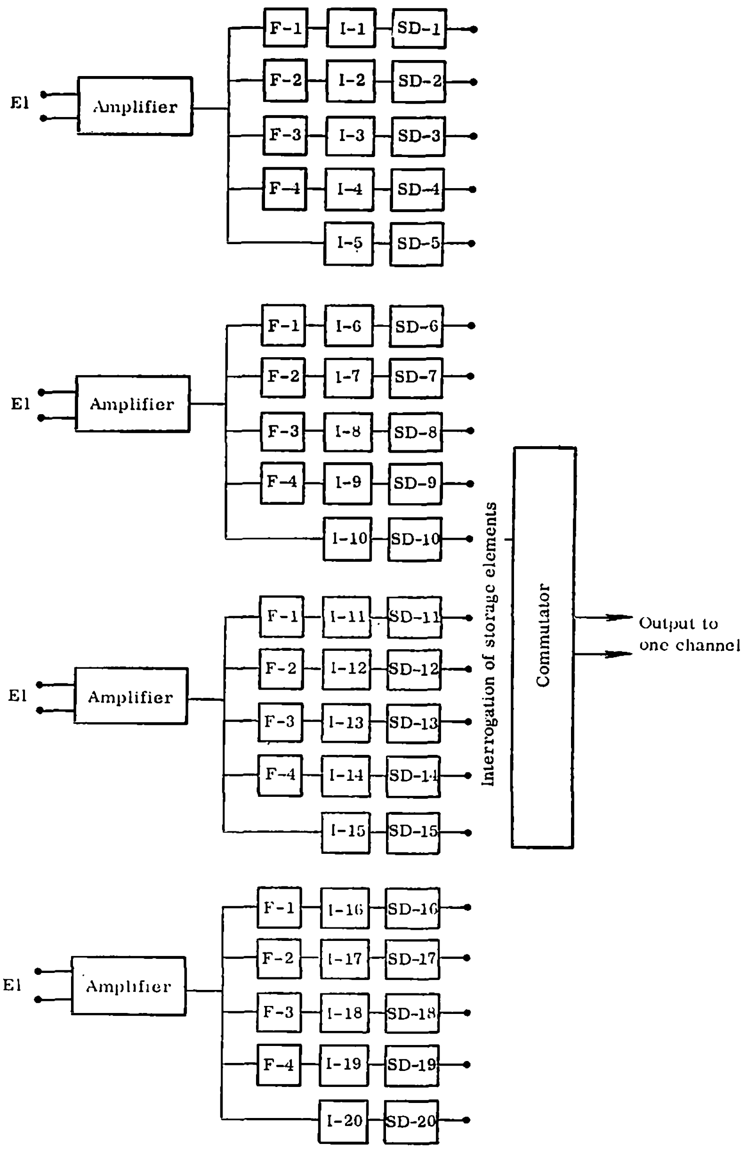


Figure 46. Block Diagram of Installation for Single-Channel Recording of Four Electroencephalogram Leads. El = Electrodes; F = Filters; I = Integrators; SD = Storage Device.

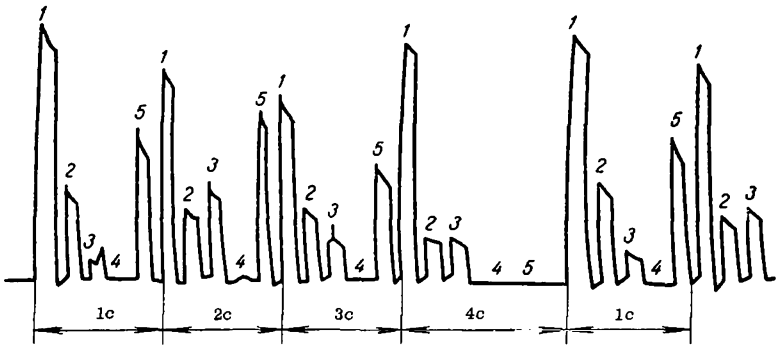


Figure 47. Sample of Single-Channel Recording of Four Electroencephalogram Leads. Bottom = Channel Designations. Top = Impulse Designations: 1 = Total Biopotential Power; 2 = Alpha Rhythm Power; 3 = Beta Rhythm Power; 4 = Gamma Rhythm Power; 5 = Delta Rhythm Power.

The use of punched cards and magnetic tapes for recording medical data is of much practical interest. A large number of overworked clinics have already made the transition to punched-card case histories. This makes it possible to quickly process data with the aid of computers, to set clinical precedents, and to perform calculations. We have punched cards for recording medical information which are being used only in a number of large specialized institutions that conduct scientific research work on the application of computer technology to medicine. These organizations include the A. V. Vishnevskiy Institute of Surgery in Moscow [2], the Polenov Institute of Neurosurgery in Leningrad, and the clinic directed by Professor N. M. Amosov in Kiev.

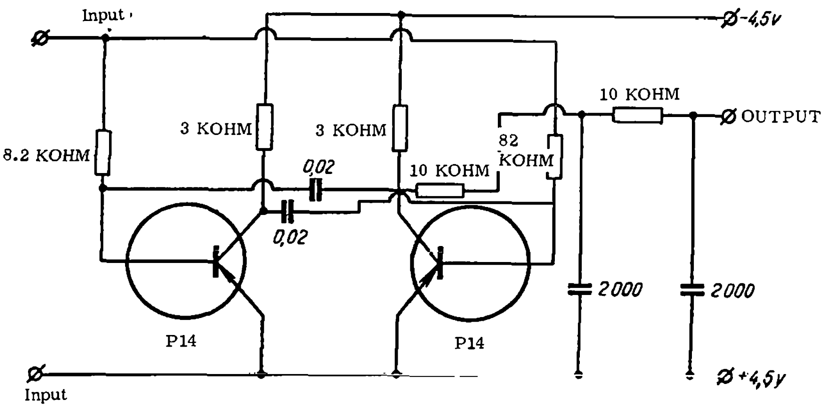


Figure 48. Multivibrator for Recording Physiological Parameters on Magnetic Tape.

Magnetic recording also is not established at the present time in the /161 clinics and laboratories. The universal magnetic recorder (two-channel) manufactured by the special design bureau "Biofizpribor" in a limited quantity, in spite of its rather good operating characteristics [3], is extremely bulky.

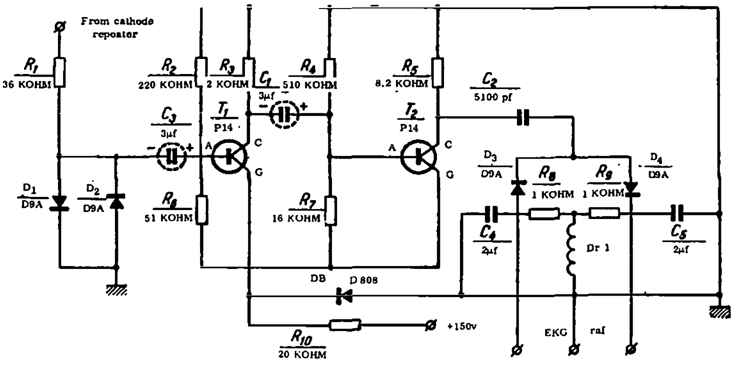


Figure 49. Frequency Meter-Decoder [E. I. Rimskikh].

A standard tape recorder can be used to record almost any physiological parameter. The recording is made on a carrier sound frequency. It is best to use a multivibrator as a modulator (Figure 48). A voltage of 0.5-2.0 is fed into the /162 output of the multivibrator from the next to the last amplifier stage of the series instrument (electrocardiograph, electroencephalograph) or from special amplifiers. Information that is recorded on magnetic tape may be analyzed visually, transcribed to paper tape or film, or fed directly into a computer. The devices developed by E. I. Rimskikh [4] (Figure 49), for example, may be used as demodulators.

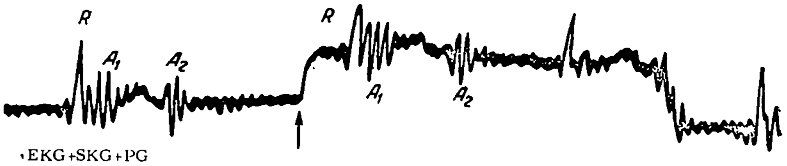


Figure 50. Combined Tracing of Electrocardiogram, Seismocardiogram, and Pneumogram. R = Electrocardiogram R-Wave; A_1 and A_2 = Seismocardiogram Oscillatory Cycles. Arrow Indicates Beginning of Inspiration.

The shortcoming of standard tape recorders is that they are only single-channel. The Yauza-10 stereophonic tape recorder can be used to simultaneously record two parameters. A special attachment can be devised for a tape recorder which makes it possible to record two subcarrier frequencies on one track. The method of combined recording of several parameters over one channel was developed for the purpose of expanding the capabilities of using magnetic recording in clinical medicine and physiology. This method is not suitable for research purposes, but is quite applicable when it is necessary to provide operational medical monitoring. Figure 50 illustrates a combined tracing of an electrocardiogram, seismocardiogram, and pneumogram. It is easy to recognize practically every characteristic of the indicated parameters in this tracing. A combined tracing can be fed into digital computers directly or from magnetic tape. For magnetic recording of data which are expressed numerically or some other way, a code in the form of various voltages fed to the modulator input can be used.

Questions concerning the collection of medical information are closely related to problems of introducing computer technology to medicine and biology. Data processing on digital computers can be effective only if standard algorithms and programs are compiled and extensively used. There should be a library of /163 standard programs recorded in the universal machine language "Algol-60". If all data processing is standardized, its results will be compatible and it will be possible to establish universal archives of medical information, i.e., a veritable depository of science and practice. We will return to the question of medical archives later; it should be noted here that only unified methods of information collection can create the prerequisites for standardizing data processing and storage. Standardization of information collection means that any data on a patient are recorded strictly on the basis of a standard program. There should be a sufficient quantity of these programs and they should be governed by various diagnostic algorithms.

The programming of medical information collection will also make it possible to reorganize the examination of patients and to extensively automate this process. A medical research program is a time chart of the recording of a list of parameters with an indication of the sequence and character of functional tests. Two types of programs can be distinguished: general medical programs and specialized programs.

A general medical program simulates the diagnostic approach of the attending physician who admits the patients. It is his duty to give first aid, to determine the need for a specialized examination, and to make a tentative diagnosis. The general medical program should thus include a rather diverse list of investigations sufficient for the obtainment of information on the performance of all the main systems of the organism. Programmed information collection denotes not only the application of instrument methods with objective recording of the appropriate oscillograms, but also the acquisition of data obtained by questioning the patient and by investigations conducted by the physician. A special project concerned with automatic diagnosis solely based on a patient's complaint data may be cited as an example [N. Brodmen, 5]. A questionnaire composed of 195 questions, each of which requires an answer in the form of "yes" or "no" is used. The questionnaire standardizes the examination and makes it possible to work out a general diagnostic algorithm. Simulation of the diagnostic process on a computer after the appropriate "instruction" has made it possible to obtain extremely interesting results. Thus, when data obtained from questionnaires were analyzed simultaneously by an experienced physician and by a computer, the number of correct and incorrect diagnoses in 350 patients was approximately identical for the physician and the computer. The patient's /164 questionnaire is actually nothing more than a programmed collection of information.

Specialized programs differ from the general medical programs by the fact that they simulate the diagnostic operations performed by physicians with very confined specialities: e.g., neuropathologists, endocrinologists, ophthalmologists, etc.

Questions of information collection are important not only as the first stage in automating the analysis and evaluation of medical data, but they are also of independent interest. Too much of the physician's time today is spent in the collection of information, while the speed of obtaining the necessary information and the possibility of active control of information retrieval are very poor as compared to the information methods employed in other fields of science and technology. Cybernetics is opening new paths for optimizing the processes of collecting medical information. Automated and programmed information collection, and the development of methods for optimum representation of the necessary data will make it possible in the near future to provide the physician with additional time to accomplish his chief function: interpreting the data obtained in order to make the most effective decisions.

Information Analysis

The analysis of medical information entails an extremely diversified series of tasks: from the simple interpretation of oscillograms to the performance of a correlation analysis, which requires a special technical base.

By analysis, we mean the stage of a diagnostic process which is associated with the preparation of collected information for logical or mathematical evaluation, the result of which is the "diagnosis". Thus, the electrocardiogram is the primary basis, for example, for making the diagnosis, "coronary artery atherosclerosis", and is then subjected to the appropriate analysis. The various time and amplitude indices are calculated first, pecularities in the tracing are noted which distinguish it from the known normal types of electrocardiograms, then all of these data are summarized, compared with the data of clinical observation and the patient's complaints, and finally a diagnosis is made. Deviations are often so expressed that a diagnosis can be made literally "at first sight", e.g., the electrocardiographic picture of myocardial infarction is frequently very indicative. This does not mean, however, that there is no information analysis stage in the diagnostic process. This stage occurs very /165 quickly and is not noticed by us simply because of the distinct deviations. The diagnosis is not so clear in the majority of cases and requires tedious analysis of data. Machine methods of analysis with the application of statistics and mathematics are useful in this case with respect to the speed of processing a large volume of information, as well as with regard to providing qualitatively new results which essentially facilitate a diagnosis. Thus, for example, mathematical methods of electroencephalogram analysis [6] have been used extensively in the last few years with the application of automatic devices, as well as correlation analysis of electromyograms [7], frequency analysis of electrocardiograms [8], and other methods.

The main task of analysis is to eliminate information redundancy on the one hand, and to extract hidden information on the other hand. In summary, the final purpose of analysis is the optimum representation of information in a form which is most applicable for performing the following stages of the diagnostic process.

We can conditionally designate three stages in the analysis of medical data.

1. Interpretation or conversion of data into digital form.

2. Statistical and mathematical treatment of the data.

3. Comparative analysis of the data (comparison of the quantitative characteristics obtained with certain constants).

The first stage in the analysis of medical information, i.e., interpretation, is often a procedure associated with the participation of the person who reads the data during the process of measurement. Characteristic elements of a curve may be identified during interpretation, individual primary indices determined, and finally, certain dependent, secondary indices are calculated. Interpretation is the most critical and tiresome part of analysis for the operator, since it requires from him, in addition to knowledge and experience, a great deal of mental strain. Interpretation errors affect the entire subsequent course of analysis.

Attempts are presently being made to automate the interpretation of oscillograms. Semiautomatic and automatic systems are in existence. Semiautomatic systems free the operator from the task of reading the recording or the computations, but he still retains the identification function. One method of semiautomatic interpretation consists of using a keypunch machine. The values read by the operator in this case are fixed on punched tape or punched cards, and /166 the entire subsequent analysis of the data can be performed by computers.

Special reading devices have been developed for automatic interpretation. The Kiev Polytechnic Institute has designed a photo-optical electronic device which reads graphic functions from tapes [9]. This device makes it possible to convert graphic data into electrical signals for subsequent processing in computers. The instrument is a servo system which has the position of a curve on a graph at its input and a voltage corresponding to this position at its output. The instrument operates by means of the reflection of a luminous flux from a carrier with a graphic function. The design of the instrument combines two known readout methods: the servo method and the scanning method. Recordings on magnetic carriers are more suitable for readout with automatic interpreting devices.

Questions of automatic data readout from various types of carriers are very important to the further development of medical science and practice. The introduction of reading devices and information converters would make it possible to release a large number of laboratory technicians and physicians for creative work. Successful attempts are now being made with regard to the automation of laboratory investigations (see Chapter V). As an example of a solution to the problem of automatic data readout in an x-ray study of the cardiovascular system, we shall describe the instrument developed by Becker et al. [10]. With one of the important chest x-ray indices as their basis, i.e., the ratio of the maximum transverse diameter of the heart to the maximum transverse diameter of the chest, the authors proposed to automate fluorogram analysis, which is very valuable in the examination of large contingents. The readout device is an electro-optical scanning converter. The fluorographic frame is divided into 160,000 elements with a grid containing 320 lines and 500 columns. Each element of the grid is coded for readout with numbers from 00 to 99, whereby 00 denotes the most nontransparent section, and 99 indicates the most transparent section. The numbers are recorded on magnetic tape in the form of electrical signals. The computer program consists of two parts. A so-called sum curve is computed first. It consists of 500 figures which correspond in sequence to the column numbers. Each figure is the sum or integral value of all lines of a given column. As a result, the "sum curve" has peaks on it which designate the transition from transparent sections to nontransparent sections, and depressions which denote the transition from nontransparent sections to transparent sections. It is easy to distinguish the margin of the costal arches and /167 the boundaries of the heart on the curve. The computational algorithm and the program are quite simple.

Automatic recognition of oscillograms is more complicated; for example, electrocardiogram waves. One variation of automatic electrocardiogram analysis will be described below. It consists of recording on magnetic tape, readout, discerning the waves, and calculating various indices [11].

The electrocardiogram, which is recorded on magnetic tape, is converted into numerical values at a rate of 625 calculations per second, i.e., one measurement every 0.0016 second. A recording with a duration of 5 seconds is selected for analysis. The electrocardiogram is fed into the computer in the form of a sequence of figures. The first recognition procedure is finding the R wave. To do this, the first derivative is calculated and its maximum negative deviation is determined. The peak of the R wave is determined as the point from the maximum positive amplitude before the maximum negative deviation of the derivative. The P and Q waves are found as the points with minimum amplitude after the maximum negative deviation and before the peak of the P wave, respectively. The logic employed in the recognition of all waves and intervals of the electrocardiogram is based on certain rules which represent the regularities in the relationships between curve elements. Thus, the origin of the T wave is determined as the first positive or negative deflection of the curve after the end of the S wave, which exceeds the value of 0.01 mv per 0.01 second.

The second stage in the analysis of medical information consists of statistical and mathematical treatment. The simpler methods of statistical treatment are well known to physicians and biologists.

Every physician and biologist should know how to calculate the mean deviation, the standard deviation, and the mean square error. From the standpoint of cybernetics, however, these calculations take on a new meaning. When statistically investigating the results of biological measurements, we are always dealing with a random sampling of general quantities. The variance of the data in a random sampling depends on the variations induced by the very nature of the biological objects, as well as variations associated with vital processes. At every moment of time (t_0), the condition of a biological object differs from its condition in the preceding ($t_0 - t_1$) and the subsequent ($t_0 + t_1$) moment of time. Therefore, averaging makes it possible to determine the "constant component" of the biological phenomon under investigation, but cannot charac- /168 terize its current state. The standard deviation indicates the range of most probable variations of a biological phenomenon and can be considered as a measure of normalcy (or morbidity) if the number of operations is sufficient.

If we consider biological phenomena from the standpoint of the theory of random functions, it becomes possible to apply statistical-probability methods to time processes. As we know, there are stationary random processes which are characterized by the law of probability distribution and are not dependent on time, and nonstationary random processes which are distinguished by expressed probability variations of individual operations. Thus, for example, the dynamic series of values of an electrocardiogram RR interval can be considered as a model of a stationary random process only for conditions when the test subject is in a state of relative rest. The organism is in a state of readjustment to a new functional level during and immediately after physical exercise, and in this case the dynamic series of RR intervals is not standard.

The property of ergodicity is characteristic for many stationary random processes, i.e., any statistical characteristic of this process which is obtained by means of a large number of operations can be obtained with high reliability by averaging a series of measurements over time in one single operation. This opens up new possibilities for the statistical analysis of medical information.

The mathematical expectation, dispersion, and correlation function are calculated in the analysis of stationary random processes. A mathematical expectation is a quantity which corresponds to the mean deviation when working out a series of values obtained from many operations. But the mathematical expectation is a probability criterion which indicates the expected value of the mean deviation. The mathematical expectation characterizes the probability level of functioning of a biological system. The dispersion indicates the scattering of random values. This scattering is greater, the lower the quality of regulation in the system under investigation. Thus, dispersion can be treated as a criterion of the quality of regulation in response to external disturbances [12]. Finally, the correlation function is a mathematical expression of the interrelationship between phenomena. As applied to a stationary random process of biological origin, the correlation function can be considered as a criterion of the stability of homeostatic mechanisms. If the autocorrelation reaches zero in the period $T[T = (t_0 - t_1) + (t_0 + t_1) = 2t_1]$, this means that the /169 time T was sufficient for the complete restoration of the system from disturbances that had acted upon it at the moment $(t_0 - t_1)$.

Since many biological processes can be considered as stationary random processes which possess the property of ergodicity, it becomes possible to more extensively utilize mathematical derivations in medical practice.

Various indices of circulation, respiration, and nervous activity can be analyzed with random-function methods with an accuracy sufficient for diagnostic purposes.

Having the successive values of all operations of a random process which is uninterrupted during a certain time segment, we obtain a variation series to which the methods of variational statistics can be applied. Of particular interest in this case are the distribution curves. Figure 51 illustrates the distribution curves for a series of values of electrocardiogram RR intervals in the form of a smooth variation curve and in the form of a histogram. The values of the intervals are plotted along the x-axis and their frequencies are plotted along the y-axis.

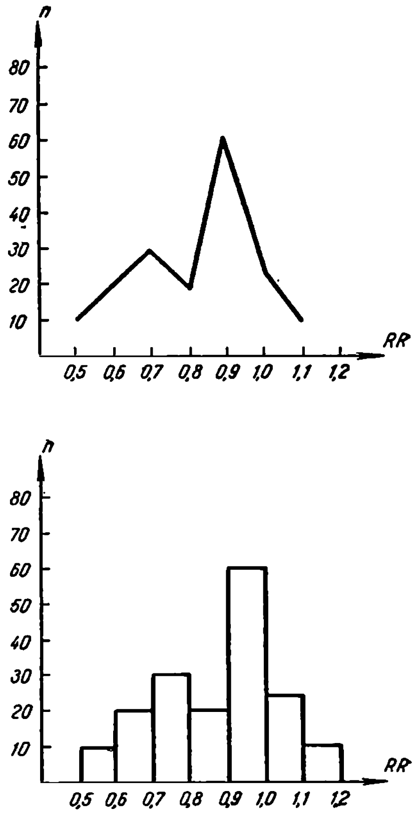


Figure 51. Variation Curve (Top) and Histogram (Bottom) of a Dynamic Series of RR Intervals on the Electrocardiogram.

There are different forms of distribution curves. The so-called normal curves are encountered most frequently. They are smooth and bell-shaped. A characteristic feature of a normal curve is the fact that its middle ($\bar{x}$) coincides /170 with the mean deviation, the mode, and the median. If the area bounded by a normal curve is taken as unity, 0.997 of this entire area will lie within the limits of $\bar{x} \pm 3\sigma$. Probability integral tables can be used to calculate the frequency of various deviations from the mean. However, an ideal normal distribution curve is obtained only if the sampling according to which the series is constructed is sufficiently close to the general set or if the random process corresponds to the ergodicity hypothesis.

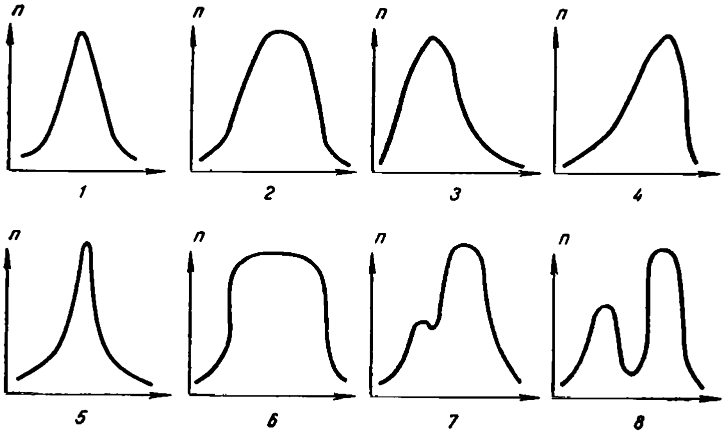


Figure 52. Types of Variation Curves.

Ideal normal curves are rarely obtained in practice. Only the first two curves can be considered to be normal in Figure 52. Curves 3 and 4 are said to be asymmetric, curves 5 and 6 are known as excessive curves, and curves 7 and 8 are multivariation curves. What is the physiological interpretation of these curves?

Asymmetric curves indicate the nonstationary character of a random process. This can mean that the stationary conditions have been disturbed in the process of investigation and some action has been rendered on the organism. Asymmetry indicates a nonsteady state, and the degree of disturbance of homeostasis can be expressed by the skew factor:

$$\left(A_s=\frac{M-M_0}{\sigma}, \text{ or } A_s=\frac{3(M-M_e)}{\sigma}, \text{ or } A_s=\frac{\mu^3}{\sigma^3}\right)$$

Asymmetric distribution curves can be obtained in the analysis of cardiac cycles during physical exercise.

Excessive curves indicate that the maximum number of realizations practically coincide with the value of the mean deviation, the mode, and the median. /171 The biological interpretation of these curves is associated with the presence of increased stability of the system to external disturbances, and internal closure of the system as it were, or, conversely, with the total subordination of the system to commands from nerve centers. A variety of the excessive curve is a curve in which the extreme values are less than 3σ. These curves also represent the stabilization of the operating conditions of a biological system, but can be considered as a sign of limited adaptability or decreased reactance. The formula $Ex = \mu^4/\sigma^4$ is used to calculate the excess. It may be assumed that the value of the excess can characterize the relationship between the processes of self-regulation and central control. The rhythm of a denervated heart provides an excessive type of distribution, just as does the rhythm during violent emotions.

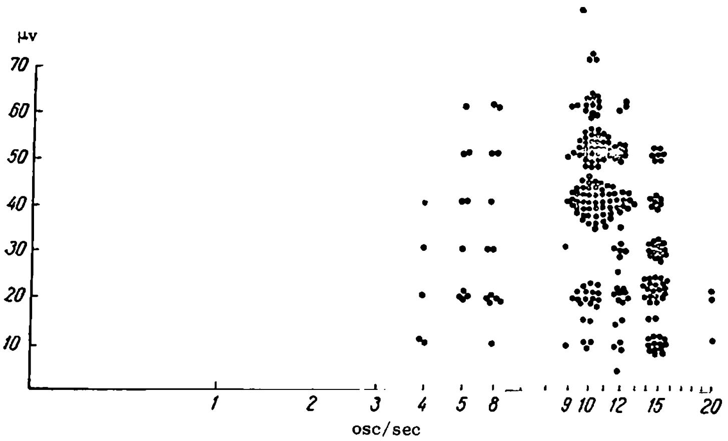


Figure 53. Histogram which Demonstrates the Statistical Distribution of Electroencephalogram Waves. Each Wave is Designated by a Separate Dot. The Frequencies are Plotted along the x-Axis and the Wave Amplitude in Microvolts is Plotted Along the y-Axis [Fora, 1953].

Multi-peak curves indicate the diversity of a variation series. They can indicate either the simultaneous effect of several processes on the value of the realizations of a random process, or that during the investigation some action took place which caused the transition of the system to a new level of functioning. The /172 cause of a double-peak distribution curve may be a so-called transgression, i.e., the presence of two independent variation series. This occurs when complex phenomena are subjected to variational-statistical analysis; for example, a series of electrocardiogram RR values recorded during a period in which there were states of physical stress and breath holding along with a state of complete rest.

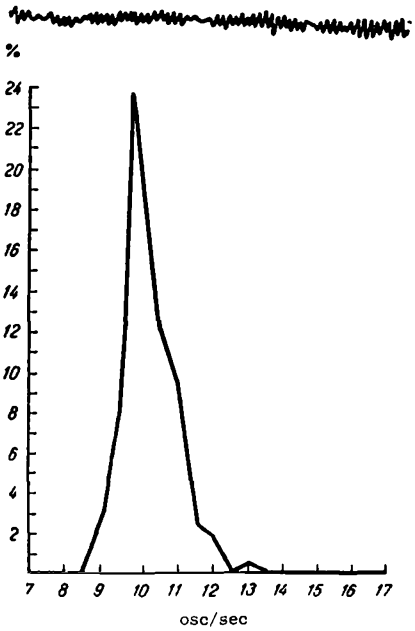


Figure 54. Histogram of Normal Human Encephalogram. The Frequencies are Plotted along the x-Axis and the Time (in Percent) Occupied by Each Frequency in the Electrocardiogram is Plotted along the y-Axis. The Original Electorencephalogram is Given at the Top [Brejer et al., 1945].

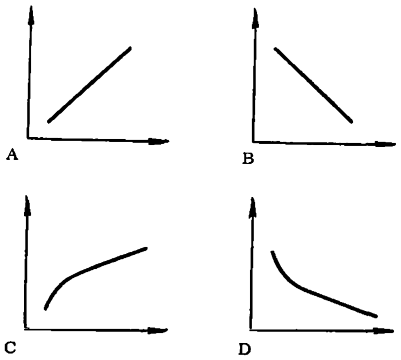


Figure 55. Types of Correlation Relationships between Biological Indices. Linear (A and B) and Nonlinear (C and D) Relationship; Direct (A and C) and Inverse (B and D) Relationship.

In spite of the fact that only variation series which satisfy the "hypothesis of normalcy" can be selected for treatment, in a strict approach to statistical analysis from the standpoint of the theory of random functions, the advantage of an a priori application of this hypothesis to various materials is obvious. The variation curve method, or as it is called, histographic analysis, has been employed particularly in electroencephalography [7]. There are several methods of constructing histograms which represent the relationship between the amplitude and frequency of a brain biopotential. According to Fora, a histogram is constructed in such a way that each wave is depicted in the form of a separate dot in accordance with its length and amplitude. The frequencies are plotted along the x-axis and the time (in percent) occupied by each frequency in the electroencephalogram [Brejer] is plotted along the y-axis. Figures 53 and 54 illustrate two of these types of histograms. Automatic instruments also have been developed for histographic analysis.

Histographic analysis in general form /173 makes it possible to explain an important characteristic of a random process, i.e., the distribution function. We have already indicated the various types of variation curves which represent the various distribution functions. An empirical variation series is obtained in the analysis of materials from biological measurements, and one of the tasks of analysis (comparative analysis) consists of constructing a theoretical variation curve which most closely approaches the obtained variation series. Various methods are employed to evaluate the degree of coincidence of the theoretical and empirical curve: e.g., Pearson's criterion (χ^2), A. N. Kolmogorov's method, etc.

One of the important tasks of the mathematical analysis of biological phenomena consists of finding the interrelationship between various indices. Biological systems are well organized and intercorrelated with regard to their internal parameters. The homeostatic function which is effectively accomplished by living organisms is ensured only due to the fact that the organism reacts as an entity, while its individual elements are subordinated to a general program of actions.

The relationship between the parameters and indices of a biological object rarely has a linear character. They are most often nonlinear complex relationships whose mathematical models are still unknown. However, even the use of ordinary statistical correlation factors has made it possible to establish what we are dealing with. What kind of interrelationship is it? Is it a direct or inverse relationship? It is linear or nonlinear? Figure 55 illustrates a few types of relationships. Methods for calculating the correlation factors and correlation ratios have been described in the majority of textbooks on statistics.

The method for calculating the correlation function is used to explain the interrelationships in time processes. This /175 function is computed by means of mathematical machines since its manual computation is extremely laborious. The method of calculating the correlation function consists of multiplying a series of values, which reproduce the given process, by the same series moved

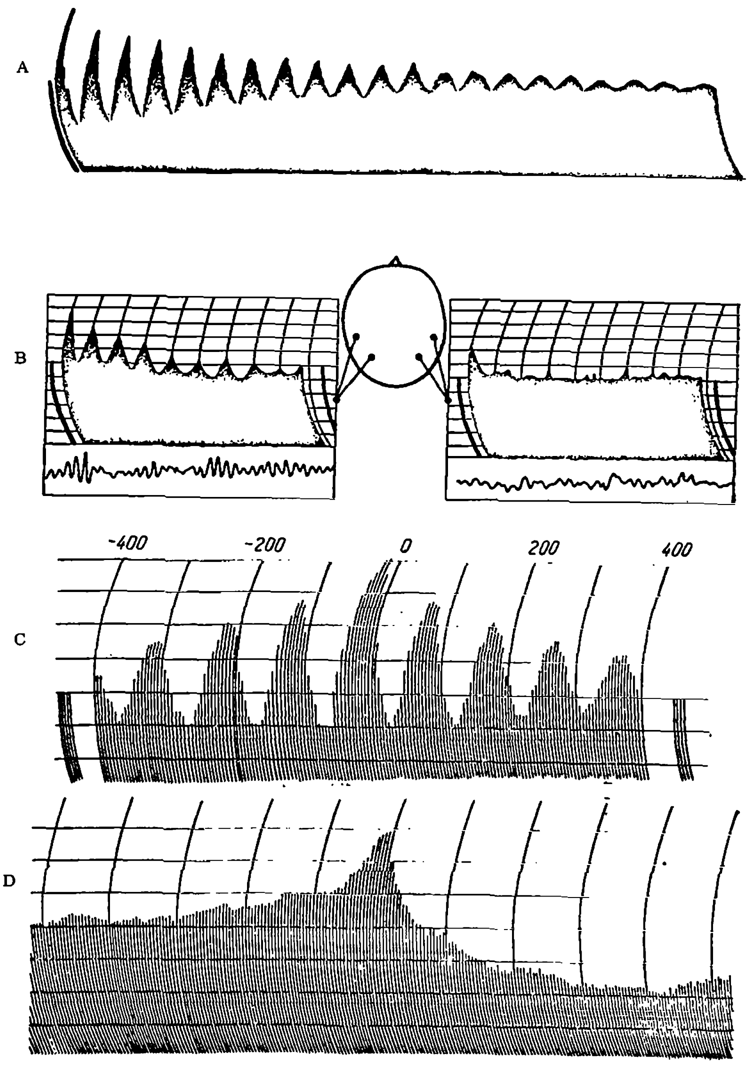


Figure 56. Correlation Analysis in Electroencephalography. A = Typical Autocorrelogram of a Normal Electroencephalogram [Brejer, 1960]; B = Autocorrelogram of a Patient with a Brain Tumor on the Right Side. Samples of Original Electroencephalograms are Given under the Graphs [Brejer and Darlow, 1956]; C = Intercorrelation Function of Electroencephalogram of Both Hemispheres of a Healthy Person. The Time Delay in Milliseconds is Indicated on Top; D = the Same Condition in a Patient with a Meningioma on the Right Side [Brejer, 1960].

along a time axis for a certain interval T. The results of multiplication are averaged and the data obtained for different values of the time shift are plotted on a graph. The time-shift intervals T are depicted along the x-axis of this graph, and the average degree of statistical correlation between the amplitudes of the process being studied is plotted along the y-axis. Figure 56 illustrates samples of various correlation functions.

These curves indicate autocorrelation functions, i.e., they are the result of comparing the process with its duplicates shifted at varying intervals. This analysis makes it possible to separate the periodic and random components of the process being analyzed and reveals the spectral composition of a complex process to a certain extent.

An intercorrelation (cross-correlation) function is obtained by comparing two functions (two processes), which makes it possible to determine the moment of time when the relationship between two processes is optimum. This is of interest especially when it is necessary to establish the dependence between reactions and certain influences or to find regular responses among random fluctuations. Cross-correlation analysis makes it possible, for example, to isolate weak bioelectrical responses of the brain against a background of expressed activity [7]. Autocorrelograms of electroencephalograms make it possible to judge the periodicity of bioelectrical processes, while cross-correlograms make it possible to estimate the phase relationships of oscillations in different leads [13]. Correlation analysis has been employed not only in electroencephalography, but also in electromyography [14], and in heartbeat analysis. The specialized EASP-S [15] electronic computer can be used for correlation analysis, or general-purpose digital computers may be employed.

Frequency analysis methods for biological processes have become very popular recently. Various types of oscillations are constantly observed in the living organism. These oscillations are both periodic and nonperiodic. Manifestation of the spectra of these parameters may have an important value for a deeper understanding of regulation and control mechanisms.

Biological rhythms are currently the subject of close study in many laboratories, whereby the transition from rhythms on the order of a few Hz, several Hz, and hundreds of Hz (electroencephalogram, electrocardiogram, electromyogram) /176 to the study of biological oscillatory processes with very long and very short periods is characteristic. Thus, for example, many investigations have been devoted to the so-called circus rhythms (daily variations). Special work is being conducted on the study of the high-frequency components of biological processes (an electrocardiogram study to 300-700 Hz and an electromyogram study to 15-50 kHz) [16, 17]. The purpose of frequency analysis is to determine the frequency components of a given oscillatory process and to find the specific gravity of each component. Frequency analysis has been employed quite extensively in electorencephalography. The practical evaluation of results of an electroencephalographic investigation is presently based on the expression of rhythms to a significant extent. The concepts of alpha, beta, delta, and theta rhythms are familiar today even to nonspecialists.

Frequency analysis of brain biopotentials was the object of special consideration by the "father of cybernetics", Norbert Wiener. In the last chapter of his book, Cybernetics, entitled "Brain Waves and Self-Organizing Systems" [18], Wiener presents the results of a harmonic analysis of the autocorrelation function of electroencephalograms (Figure 57) and points out that the curve which is obtained has a steep drop to a frequency of about 9.05 Hz. This circumstance made it possible for Wiener to express the proposition concerning the presence of a mechanism which strobes or synchronizes biopotentials that originate in various regions of the brain. There then occurs the "attraction" of different frequencies, and a single rhythm is formed. This synchronization mechanism organizes the cerebral system with respect to an increase of its stability. Variations in the frequency characteristics of the electrical indices of not only the cerebral function, but also the function of the muscles [19], the heart [16], and the peripheral nervous system [20] are presently being evaluated quite definitely in connection with the variation of the functional state.

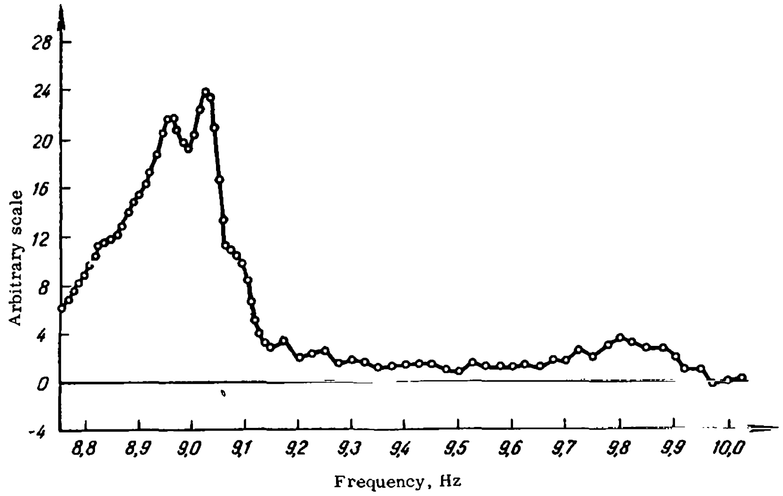


Figure 57. Spectrum of Normal Electroencephalogram [N. Wiener].

Frequency analysis is beginning to be employed for the analysis of diverse physiological functions. Ye. I. Pal'tsev [21] has indicated that the spectral composition of a tremor varies as a function of the character of the motor task. L. B. Andreyev and his coauthors [22] have demonstrated the diagnostic effectiveness of the harmonic analysis of kinetocardiograms. With regard to the slow and ultra-slow biological rhythms, they are presently being studied intensively by various specialists. The slow rhythms of brain biopotentials have been investigated by N. A. Aladzhalova [23]. A great deal of work has been devoted to /177 heat-regulation rhythms [24]. The problem of the "biological clock" is closely related to the study of the rhythmic nature of biological processes.

An interesting attempt at the mathematical examination of the properties of biological oscillatory systems was made by C. Clotter [25]. He considers two types of systems: autonomous and nonautonomous. Autonomous systems may have damping (not capable of self-oscillations) or may be undamped (capable of self-oscillations). In the second case, the energy dispersed in the course of a cycle is restored by a nonperiodic source. Nonautonomous systems accomplish forced oscillations in accordance with the frequency of the master oscillator. An important role is evidently played by the phenomenon of pulling, when the forced oscillations suppress the natural oscillations. This occurs when the frequencies of the natural and forced oscillations are close to one another. In the example given above from the last chapter of Cybernetics by Norbert Wiener, the appearance of a peak at one of the frequencies near 9 Hz is explained mainly by the process of pulling. The pulling region characterizes the stability of the system. Thus, experimental methods of studying dynamic spectral characteristics make it possible to evaluate a number of important parameters of biological systems. We should also mention the importance of spectral analysis for the investigation of phase relationships and synchronization processes in biological systems.

We have especially emphasized the little known aspects of frequency analysis since its application in electroencephalography, electromyography, and phonocardiography has been covered quite extensively in medical literature. /178

Differentiation and integration methods have recently been employed in biology. In differentiation, the rate of change of a process per unit time is determined. The rate component is of much interest for the study of biological regulatory mechanisms.

The investigation conducted by M. Kleins [26] indicated the presence of unidirectional rate sensitivity in biological systems. For example, the tactile analysor, after the finger touches a familiar object, provides specific information only at the moment of contact. Adaptation then occurs and no longer is any information given. An organ which is sensitive to a change in speed produces differentiation in the mathematical respect. Thus, investigation of the rate components of biological reactions will enable us to gain a deeper understanding of the mechanisms of living objects. /179

R-C circuits with the appropriate parameters are used to differentiate biological processes which are represented in the form of electrical voltage. The R-C product is called the time constant and differentiation occurs only if the time constant is less than the duration of one period of the process under investigation. Additional information is obtained as a result of differentiation. Thus, ballistocardiography extensively employs speed curves which make it possible to reveal many deviations which are not detected when recording motion. An acceleration curve is obtained by binary differentiation.

Figure 58 illustrates examples of ultralow-frequency ballistocardiograms of movement, speed, and acceleration. These curves are not only externally different, but they also have different physical meanings. The movement curve represents the variation in the general center of gravity of the body. The speed curve makes it possible to estimate the quantity of motion transmitted by the heart to the body. The acceleration curve indicates the power ratios in the cardiac cycle [27]. Sphygmograms, dynamocardiograms [28], and other physiological recordings are now being differentiated. The derivative is calculated according to special standard programs when digital computers are used. It should be borne in mind that certain data sensors themselves record derivatives; thus, electromagnetic pickups record speed curves:

$$(\Phi = -\frac{dw}{dt}).$$

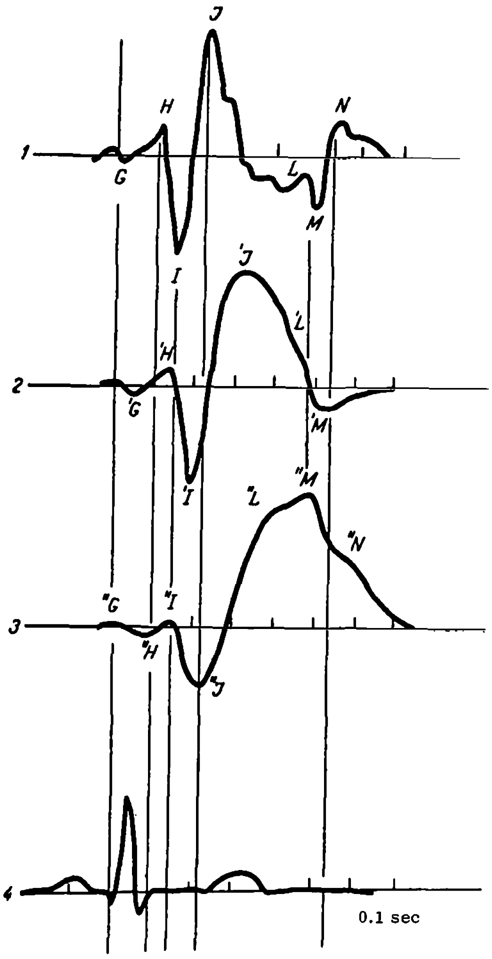
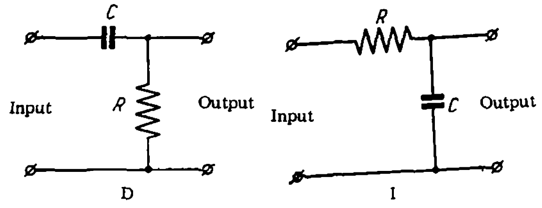


Figure 58. Ultralow-Frequency Ballistocardiograms of Movement (1), Speed (2), and Acceleration (3) [Scarborough and Talbot].

Integration is employed when it is necessary to evaluate a large number of similar data in a certain time interval. Various integrators are used in electroencephalography to determine the average power of bioelectric potentials in a given frequency range. Methods /180 have been developed for long-term integration of brain biopotentials, mechanical manifestations of cardiac activity, and other physiological processes [29]. There are methods and instruments for determining the total pulse rate in days [30]. This is also a unique form of integration. An integration method is used to calculate the areas under a curve. A simple integration circuit consists of a capacitor and a resistor as depicted in Figure 59. Integration can be performed with a digital computer on the basis of special programs. Integration is employed when it is necessary to derive a general impression of a process on the basis of its particular attributes.

Of the mathematical methods which are gradually being employed in biology, we might mention the methods based on probability theory, information theory, and games theory [31]. Attempts have been made to calculate the entropy of pulse rate [32].



D I

Figure 59. Differentiating (D) and Integrating (I) Circuits.

The third stage in the analysis of medical information consists of comparing the obtained statistical, mathematical, and other indices with known constant indices. When a physician examines a patient, he compares each physiological index with the data which, in his opinion, characterize the norm. Thus, the result of a comparative analysis performed by a physician depends on the accuracy and validity of the measurements, and on the correctness of the norm indices selected by him. It should be taken into account, however, that the norm is a dynamic concept. A pulse of 100 beats per minute is clearly abnormal for a human being at rest. If, however, this figure is obtained in the first minute after moderate physical exercise, it causes no apprehension. Consequently, the physician's brain must select those constants which optimally correspond to the situation for a given case. The correct analysis of data, and consequently, an effective diagnosis are possible only on the basis of a perfect knowledge of norm alternatives.

The paradox of the development of modern medicine, however, consists in the fact that all the efforts of clinicians and physiologists are directed toward the manifestation of various signs of disease, as a result of which it turns out that we know more about what is "bad", and do not know where the "good" leaves off. The latest reference aid on physiological constants, written by S. Pawelski and Z. Zawadski [33], presents data which characterize the most diverse indices of the human organism. These constants, however, are static, and they refer only to conditions of rest. Attempts to establish "norms" for physi-/181 cal conditioning are contained in the works of V. B. Malkin [34]. He proposes the introduction of the "stress-norm" concept, which denotes that a given index is normal under the conditions of a given action.

The intercorrelation of biological processes in the organism condition the close relationship between some indices and others. If for some reason a change occurs in one of the indices, the regulatory and homeostatic mechanisms immediately bring the other indices into accord with the first. This means that the "norms" for all indices vary. Acquired conditions even have their own norms. For example, a subfebrile temperature in pneumonia does not suggest any danger, while a sharp increase in temperature to 41-42° compels the physician to take timely measures: it is a normal reaction for leukocytosis and a danger sign for lymphopenia.

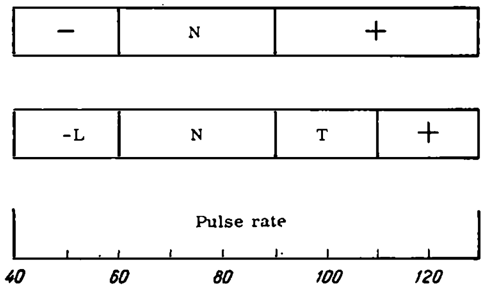


Figure 60. Methods of Representing "Norm" Limits for Some Physiological Indices.

Thus, the comparison of the obtained /182 data with constants is the concluding and most critical stage in the analysis of medical information. Automation of this stage of analysis is feasible and even desirable, since a machine "memory" is more "reliable" than the human memory, and the high speed of a machine provides a highly effective comparative analysis, which permits the selection of the most appropriate constants for the given case and makes it possible to quickly calculate the degree of distinction and similarity. If we use the binary logic of comparison as our basis, i.e., we answer "yes" or "no" to the question of the similarity between a given index and a given constant, machine analysis will then provide for the application of more exact probability methods.

Constants may be assigned by different methods. Some of the simpler methods

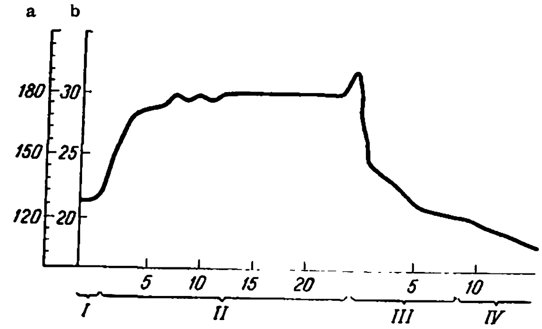


Figure 61. Pulsogram of a Skater. Prestart (I), Run (II), Recovery (III), and Rest (IV). Recorded by means of Radiotelemetry Equipment [V. V. Rozenblat, 1960]. a = Pulse Rate in Minutes; b = Pulse Rate in 10 Seconds.

are depicted in Figure 60. A scale made up of 3, 4, or 5 areas is devised, whereby each index has normal, transient, and limiting values expressed in figures. This method of assigning norms for monitoring the state of an organism under dynamic conditions requires several scales which correspond to various conditions of investigation. For example, scales are required to monitor the condition of a skater in the prestart period, the start, the middle, the end of the run, and the post-finish (Figure 61). Norms also can be assigned in the form of a continuous curve, whereupon the index values are plotted along the y-axis, and the time and action values are plotted along the x-axis. Today, however, we do not have the data available to construct similar "norm" graphs. Automatic servo systems could very effectively monitor the state of many parameters simultaneously in the /183 presence of a continuous "physiological indices--time" function. Mathematical models are more effective for purposes of analysis since they make it possible to predict the dynamics of observable shifts. It should be noted that analysis based on the comparison of two graphs (given and current) has been employed for automatic electrocardiogram processing [35]. The patient's electrocardiogram (in digital form) in this case was compared with a set of normal and pathological curves contained in the machine memory.

The most significant data for subsequent diagnosis is isolated from the total flow of information as a result of comparative analysis. The total volume of information is sharply decreased (redundancy is eliminated). In medical practice, however, the presence of a norm is sometimes just as important as pathology. Therefore, the result of a comparison of current data with constants should be considered in every case. An example of a simple instrument which is based on the comparative analysis of current information is the "Ritm-1" [36]. This instrument makes it possible to compare each RR interval of an electrocardiogram with the "conditioned normal" interval, which is calculated as the mean value for the proceeding 5-6 minutes. When the current interval deviates from the norm by more than 20%, an S or L signal is formed depending on whether the given interval is shorter or longer than the norm. An N signal (norm) is formed in the opposite case. Words are formed from the letter signals, each one having three letters. Nine different diagnoses are made from the 27 possible words (3^3): e.g., SSL = extrasystole with compensatory pause, LNN = block, and SSS = tachycardia. Thus, the instrument performs all three stages of analysis: it computes the value of the index, statistically processes the variation series of RR intervals to obtain the mean value, and compares the mean and current RR values. The formation of diagnostic signals (letters and words) is a stage of information evaluation.

A distinctive feature of automatic devices for comparative analysis is the presence of a "memory". In some cases it is a permanent memory, where different constants are recorded together with their program; in other cases it is an immediate-access memory, as is the case in the "Ritm-1" instrument, where the constants are varied in accordance with the current condition of the patient.

The analysis of medical information by a physician is also associated with the presence of two types of constants: stationary and dynamic. Unfortunately, physicians primarily use stationary constants since the human brain does not /184 possess the necessary high speed for rapid and error-free calculation of dynamic constants. Dynamic constants are criteria which should be the "norm" standards for a given specific patient. Significant changes in all the regulatory mechanisms of a patient lead to the fact that the concepts of "norm" and "pathology" take on entirely different aspects. The success of some physicians may consist in the fact that they know how to intuitively or empirically analyze information on a patient quickly on the basis of acquired knowledge and experience by using correct criteria.

The comparative analysis of medical information is one of the most critical stages of the diagnostic process. At the same time, it is the least developed area of diagnostics. It should be mentioned that a great deal of formalization must be accomplished in the area of comparative evaluation before any significant automation can be introduced. However, the physician will still have to select the basic criteria for a comparative analysis and work out the algorithm regardless of the extent of automation.

Information Evaluation

The final stage of the diagnostic process exists in the evaluation of the collected and analyzed data. The result of this evaluation is the diagnosis.

A diagnosis involves a number of statistical, mathematical, and logical procedures which are accomplished by each physician as a single psychoanalytical act.

The following items take part in this act:

a) Data on the patient (test subject), free from redundancy and represented in a form that is suitable for subsequent logical evaluation (e.g., "pulse above normal", "body temperature below normal", "WBC above normal", etc.), i.e., an appropriate set of symptoms;

b) The physician's medical experience and knowledge, acquired as a result of study and practice. Information on the most frequently encountered diseases, symptoms which define given diseases by a single criterion, the probability of appearance of a given symptom (sign) in certain diseases, etc.;

c) Laws of medical logic worked out as a result of studying medical experience and the practice of individual physicians.

We will not attempt to reveal the regularities of the diagnostic process /185 as a psychoanalytical act. This would go beyond the limits of our subject. This process may be represented from the standpoint of cybernetics as an action which is performed by a "black box". In accordance with the "black box" concept, we should designate the data on the patient and the physician's medical knowledge as the "inputs", and the diagnosis as the "output" of the "black box". The laws of medical logic must be placed inside the "black box" since they also are the basis of the diagnostic algorithm which governs the processing of information in the "black box".

Thus, the problem of automating the diagnostic process can be reduced to the simulation of a "black box". The main task in this case is to devise algorithms which would possess the necessary effectiveness. Many investigations devoted to the development of so-called diagnostic machines essentially involve searches for the best information-processing algorithms.

The use of technical means for realizing the selected algorithms is stipulated by the appropriate formulation of the problem, the number of measurements, and economic factors. One of the first diagnostic machines was devised by the French physician, Pechat (1956). The work of the American scientists, R. S. Ledly and L. B. Lusted [37], played an important role in the development of diagnostic algorithms. The first research conducted in the Soviet Union on automation of the diagnostic process was carried out by a group of Kiev scientists (B. V. Gnedenko, N. M. Amosov, and Ye. A. Shkabara) and the cybernetics laboratory at the A. V. Vishnevskiy Institute of Surgery of the Soviet Academy of Medical Sciences (M. L. Bykhovskiy, A. V. Vishnevskiy, et al.). There are presently a large number of publications on the application of digital and analog computers for diagnostics, and also on special electronic logic devices for medical monitoring and diagnostics. Since the description of even a small portion of the diagnostic systems proposed by different authors would occupy a significant volume and would hardly be useful from the point of view of generalizing the data accumuated in this area, we shall first mention the characteristics of the main types of diagnostic algorithms with illustrations and specific examples of existing instruments and devices, and then give a rather detailed description of some of the more typical diagnostic systems.

A. Diagnostic Algorithms /186

We shall conditionally define a diagnostic algorithm as a set of rules (or limitations) which determine the order of processing medical (biological) information to solve the problem of making a diagnosis. In the strict sense of its meaning, the diagnostic algorithm encompasses the collection, analysis, and evaluation of information. The diagnostic algorithm is a complex algorithm which is made up of a combination of more elementary algorithms. Information analysis algorithms are principally numerical algorithms in which quantitative operations are predominant. Logic operations play a major role in information evaluation algorithms; therefore, they may be called logic algorithms.

In this section we shall primarily consider the logic principles of algorithm construction for the evaluation of information. The following section will also contain a complete description of diagnostic algorithms together with a description of some typical diagnostic systems.

a) Matrix (Tabular) Algorithms

As we know, there are diseases which can be diagnosed quite easily on the basis of a simple set of symptoms. Table 5 presents the symptom complexes which are characteristic for severe shock, perforative peritonitis, myocardial infarct, and acute circulatory insufficiency [Neotlozhnaya pomoshch'. (First Aid.) Edited by Professor A. S. Shvarts and E. A. Nikitin. Saratov, 1960].

TABLE 5. SYMPTOMS OF CERTAIN ACUTE DISORDERS.

Myocardial infarct	Shock (third degree)	Perforative peritonitis	Acute circulatory insufficiency
sharp pain in heart region	extreme pallor	difuse pains in entire abdomen	general weakness, dizziness
vomiting	general retardation	extreme tension against abdominal wall	increase in respiratory rate, difficult breathing
increase in temperature at end of first day	decreased body temperature	abdominal distention	increase in pulse rate
moderate leukocytosis (by second or third day)	weak pulse, tachycardia	increase in body temperature	chest pains
disturbance of cardiac rhythm	decreased arterial pressure	significant increase in pulse rate	cardiac dilatation
increase in arterial pressure during first few hours of disease	breathing frequent and shallow	decrease in arterial pressure	dullness of heart tones
friction murmur	reflex inhibition	facial pallor	decrease of arterial pressure
electrocardiogram variations	decrease in erythrocytes and hemoglobin in the blood	leukocytosis	skin pallor
dullness of heart tones		general retardation	

An examination of this table, even by an individual without a medical education, indicates that the symptoms of the indicated disorders are quite diverse and, it would appear, a differential diagnosis would not be very difficult. However, an experienced physician knows that disorders very rarely occur in precise accordance with the descriptions given in the textbooks. In other words, the algorithms of a diseased organism are significantly more variable and complex than their descriptive models which are studied by physicians. In his practice, the physician constantly corrects the knowledge (e.g., diagnostic algorithms) which he has acquired in the institute. Therefore, the set of symptoms given in the table coincide with those of a patient only if the disorder develops in the classical manner. Let us assume that we are dealing only with these types of disorders and are working out methods for automating their diagnosis. Table 5 can then be converted into a "symptom-disease" matrix, /187 which is a unique diagnostic algorithm (Table 6). This table can be technically effected in the form of a relay circuit, a diode matrix, or a computer program. We shall not discuss the problems of feeding information into such a technical device (diagnostic machine) and shall conditionally represent the input system as a set of toggle switches (the "on" position (1) indicates the presence of a symptom; the "off" position (0) indicates the absence of a symptom).

Similar systems follow a rigid program. The logic of this program may be said to be deterministic. The simplicity of deterministic logic in a number of cases does not make it possible to establish a reliable diagnosis since it is necessary that there be a complete correspondence between the given signs and the signs which characterize a given symptom complex or disorder. The noncoincidence of only one sign will make it impossible to establish a diagnosis. However, rigid diagnostic systems with deterministic logic can be used quite ex- /188 tensively in the solution of many medical problems, particularly problems of medical monitoring, expert-testimonial problems, and problems of differential diagnostics.

TABLE 6. MATRIX METHOD OF ASSIGNING A DIAGNOSTIC ALGORITHM

No.	Symptoms	Diagnoses			
		Myocardial infarct	Shock (third degree)	Perforative peritonitis	Acute circulatory insufficiency
1	pains in heart region	1	0	0	1
2	abdominal pains	0	0	1	0
3	increase in temperature	1	0	1	0
4	decrease in temperature	0	1	0	0
5	leukocytosis	1	0	1	0
6	disturbance of cardiac rhythm	1	0	0	0

TABLE 6. (Continued)

No.	Symptoms	Diagnoses			
		Myocardial infarct	Shock (third degree)	Perforative peritonitis	Acute circulatory insufficiency
7	increase in arterial pressure	1	0	0	0
8	decrease in arterial pressure	0	1	1	1
9	friction murmur	1	0	0	0
10	electrocardiogram variations	1	0	0	0
11	skin pallor	0	1	1	1
12	general retardation	0	1	1	0
13	increase in pulse rate	0	1	1	1
14	increase in respiratory rate	0	1	0	1
15	reflex inhibition	0	1	0	0
16	tension in abdominal wall	0	0	1	0
17	abdominal distension	0	0	1	0
18	general weakness, dizziness	0	0	0	1
19	cardiac dilatation	0	0	0	1
20	dullness of heart tones	1	0	0	1

If we have a large number of signs, up to 2000 for example, which must be analyzed in reference to several hundred disorders, the problem of a differential diagnosis is not within the grasp of any physician [3], especially if a rapid response is required. It is natural that the deterministic approach will result in the coincidence of signs only for disorders which have a very typical pattern (with the proper collection of information). Deterministic logic, however, also makes it possible to exclude all disorders which are impossible for the given symptom complex and to select the most probable ones from the remainder. /189 This can be done by computing the number of coincidences of the available signs with the given program. The diagnosis is made on the basis of the optimum number of coincidences.

Let us consider this principle in an example with our table. We shall assume that patient A has the following set of symptoms: pains in the heart region (No. 1), increase in temperature (No. 3), increase in arterial pressure (No. 7), disturbance of cardiac rhythm (No. 6), increase in pulse and respiration rates (Nos. 13 and 14), and dullness of heart tones (No. 20). Patient B has a different combination of symptoms: pains in the heart region (No. 1), decrease in body temperature (No. 4), disturbance in heartbeat (No. 6), decrease in arterial pressure (No. 8), increase in pulse and respiration rates (Nos. 13 and 14), and dullness of heart tones (No. 20). As we can see, there are very similar symptom complexes which, in all their simplicity, would require additional investigations for making a diagnosis. For example, an electrocardiographic examination and a blood test would be very important. Let us see, however, how our "diagnostic machine" would operate on the basis of these symptoms. Table 7 lists the corresponding data, from which it is clear that the machine would have made the diagnosis "myocardial infarct" for the first patient, and "acute circulatory insufficiency" in the second. It is indisputable that a sufficiently experienced physician could pick out 4 disorders from the 20 symptoms without the aid of a machine. When the number of symptoms and the number of possible disorders are greater, however, the assistance of an automatic system which operates even on the basis of extremely simple deterministic logic is very desirable. This sort of automatic system would be especially important at first aid stations, in the receiving wards of large hospitals, and in polyclinic departments.

TABLE 7. EXAMPLE OF THE APPLICATION OF DETERMINISTIC LOGIC FOR THE DIAGNOSIS OF DISORDERS (SEE TEXT AND TABLE 6).

Disorder	Sum of positive symptoms for a given disorder	
	patient A	patient B
myocardial infarct	5	3
shock	2	4
perforative peritonitis	2	2
acute circulatory insufficiency	3	5

Simple automatic diagnostic machines are undoubtedly of interest to therapy wards with intensive care patients, to surgeons (operation monitoring), and to physiologists who conduct experiments or investigations which may place their lives in danger. Systems with devices for direct input of information from the patient are especially effective. /190

Algorithms in the form of matrices have already been employed in a number of Soviet and foreign operational diagnostic systems.

The simplest diagnostic machine which utilizes a matrix algorithm is the relay machine that was developed in Kiev at the Institute of Mathematics of the Ukrainian Academy of Sciences under the direction of B. V. Gnedenko. The operating principle of the relay machine consists of arranging the symptoms and complexes in the form of a corresponding number of parallel electrical circuits composed of series-connected contacts which close a circuit or short a resistor. If the patient's symptoms coincide with one of the circuits, a corresponding signal is generated (a light with the diagnosis number goes on). A table of symptom complexes for cardiac disorders was compiled for the relay machine on the basis of data from a thoracic surgery clinic. The table contained 90 symptoms and 156 symptom-complex variations. All of the symptoms of a given complex were connected by a logic AND conjunction. Input of the symptoms was accomplished by pressing the appropriate buttons. Thus, each line of the table corresponded to one of the branches of the electrical circuit.

The electronic logic device with direct data input may be of interest for application in hospitals and polyclinics [38].

A block diagram of this installation is shown in Figure 62. Its basic units are transducers, amplification and measurement blocks, retrieval and memory circuits, control systems, data-display units, and an indicator. Six physiological indices were selected, three of which can be measured by the number of impulses (pulse rate PR, respiratory rate RR, and actogram A) and three can be measured by the voltage level (skin temperature ST, oxyhemogram OHG, and electroplethysmogram EPG). Other parameters also may be selected. The control system provides measurement cycles from 10 to 60 seconds, and automatically connects the memory cells and sets the counters at the initial position. The diode-matrix coder is two-stage. Signals are determined in the first stage on the basis of quantity (" — " value of parameter below normal) and on the basis of the presence or absence of signals ("+" and "n"). The logic operation of comparing /191 the states of all six indices and forming a conditional diagnostic code is accomplished in the second stage. The device is designed to indicate the states of syncope, collapse, and acute cardiac insufficiency. The algorithm is given in tabular form (Table 8).

TABLE 8. OPERATIONAL ALGORITHM FOR ELECTRONIC LOGIC DEVICE

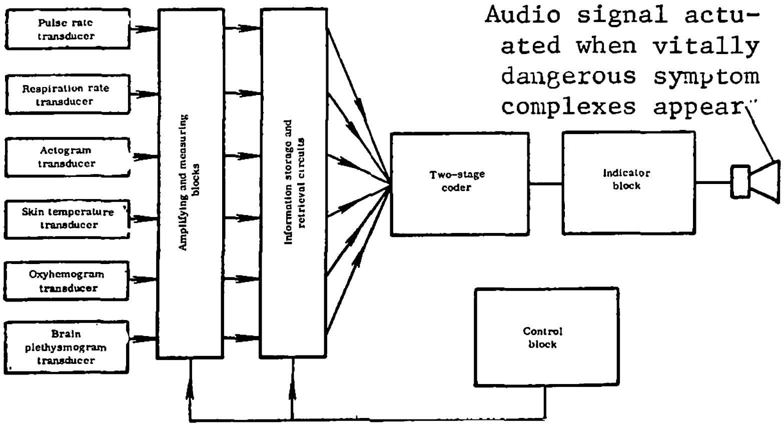
Parameters	Norm	Syncope	Collapse	Acute cardiac insufficiency
PR	n	-	+	+
RR	n	-	+	+
A	n	-	-	-
ST	n	-	-	n
OHG	n	-	-	-
EPG	n	-	-	-

A device which is used in conjunction with a digital computer is more flexible with respect to variations of the diagnostic algorithms. Small digital computers, e.g., the UM-1NKh or the "Dnepr", can be used for operations involving simple matrix logic since they can handle 10-20 patients at a time. The realization of more complex algorithms on these digital computers, however, is difficult. A special diagnostic system with direct data input and a compact digital computer was developed by R. M. Bayevskiy, V. V. Bodganov, A. M. Zhdanov, /192 and L. A. Kazar'yan [29]. The diagnostic algorithm which governs this system is expressed in the form of a block diagram in Figure 63. Table 9 gives the

TABLE 9. PROGRAM FOR THE FORMATION OF A CONDITIONAL CODE (DIAGNOSTIC ALGORITHM)

No.	Parameters	Conditional codes					
		1	2	3	4	5	0
1	pulse rate	+	+	+	±	+	n
2	respiration rate	+	-	-	±	+	n
3	pulse arrhythmia	n	n	+	+	n	n
4	mechanical work of the heart	n	±	-	n	n	n
5	skin temperature	n	+	n	n	n	n
6	motor activity	n	n	n	n	-	n
7	latent period of conditioned motor reaction	+	+	+	n	n	n
8	galvanic skin response	+	n	+	n	+	n

program matrix. Each input parameter may assume one of three states: "+" = above normal, "-" = below normal, and "n" = normal. The application of digi- /193 tal computers makes it possible to have a large number of diagnostic alternatives of conditional codes, permits them to be changed easily, and also makes it possible to vary the constants with respect to individual characteristics of the test subject.


Pulse rate transducer
Respiration rate transducer
Actogram transducer
Skin temperature transducer
Oxyhemogram transducer
Brain plethysmogram transducer
Amplifying and measuring blocks
Information storage and retrieval circuits
Two-stage coder
Indicator block
Control block

Audio signal actuated when vitally dangerous symptom complexes appear

Figure 62. Block Diagram of Electronic Logic Device (Diagnostic Machine with Rigid Operational Program).

The diagnostic system consists of transducers with amplifiers, data input and output devices, control devices, an arithmetic device, a magnetic-core immediate-access storage unit, and a long-term storage unit.

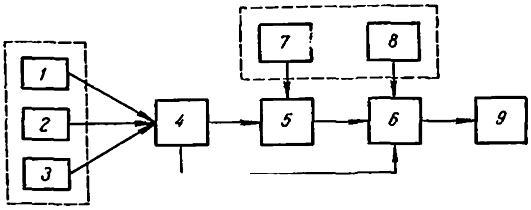


Figure 63. Diagnostic Algorithm for Digital Computer with Rigid Program. Medical Information: 1 = Questioning and Examination Data; 2 = Clinical Laboratory Data; 3 = Results of Physiological Investigations; 4 = Immediate-Access Data Storage; 5 = Comparison of Stored Data with Constants of Various Medical Indices and Given Norm Limits, Identification of Symptoms and Deviations from Norm; 6 = Comparison of Identified Symptoms and Deviations with Symptom Complexes, Selection of Symptoms and Definition of their Relationship to Specific Disorders. Machine Memory: 7 = Storage of Constants and "Norm" Limits; 8 = Storage of Symptom Complexes; 9 = Conclusions (Diagnoses).

The magnetic-core immediate-access storage unit has a capacity necessary for the storage of current data introduced during the measurement cycle, which may vary from 10 seconds to 10 minutes. The storage of information which proceeds simultaneously from all transducers requires more than 1,000 cells to record 2- and 3-digit numbers. The high speed of digital computers makes it possible to process the data during the input process, and this makes it possible to reduce the number of cells in the magnetic-core immediate-access storage unit to 32. The long-term storage unit has 256 cells for storing instructions and 32 cells for storing number constants. All signals are recorded in 13-digit binary code. The computations are performed with a fixed point.

b) Probability Algorithms

We noted above that only disorders with a complete set of given symptoms can be manifested with the aid of matrix logic. The introduction of evaluations into the sum of available symptoms increases the effectiveness of the diagnostic algorithm; however, it does not make it possible to isolate the more significant symptoms and to quantitatively determine the probability of one disorder or another. The matrix algorithm used by N. S. Misyuk and his associates [40] has been more successful. Each symptom is evaluated in this case, and its evaluation is considered in the total sum when the diagnosis is made.

The "Ural-1" computer was used to solve 132 problems associated with the differential diagnosis of brain tumors. Matrix tables were compiled for 64 diagnoses which encompassed 476 symptoms. Although the algorithm employed by N. S. Misyuk and his associates is essentially a matrix algorithm, it has also made it possible to conduct probability evaluations on the basis of a sum of "points". The symptoms are rated with their values taken into account as shown in Table 10.

The result of solving a problem was presented to the physician in the form/194 of a set of numbers which characterize the diagnosis number and the number of symptoms in each group from Table 10. If the diagnosis was not the only one possible, several diagnosis numbers were given in order of decreasing probability. The physician is able to select the diagnosis himself which, in his opinion, most closely corresponds to the clinical pattern.

TABLE 10. EVALUATION OF SYMPTOMS

No.	Symptom characteristics	Code
1	symptom very characteristic for diagnosis	3
2	symptom characteristic for diagnosis	2
3	symptom characteristic for absence of diagnosis	1
4	symptom immaterial for diagnosis	0

There are many algorithms for computational diagnostics which are based on probability criteria. The symptoms and indications of disorders in medical handbooks on diagnostics are usually accompanied by information on the frequency of their appearance for a given disease. These handbooks employ such terms as "frequently", "very frequently", "rarely", etc. The statistical characteristics of symptom complexes are now being given in separate instances, which makes it possible to estimate their probability. While the basis of diagnostics in medicine is establishing the dependence of symptoms on the presence of disorders, machine diagnostics is based on the study of the probability of the occurrence of a disease in the presence of a definite set of symptoms. The task of a probability diagnosis may be formulated as the determination of the probability of a given disease with respect to a given set of symptoms, if the probabilities of the presence of individual symptoms for specific disorders are known. The Bayes formula has been employed in computational diagnostics in connection with this problem. In spite of the intentional restriction on the use of mathematical apparatus in this monograph, which is intended primarily for physicians and biologists, we shall make an exception here and present this formula together with a detailed analysis of the methods of its application.

$$P(di/Sj) = \frac{P(di)\cdot P(Sj/di)}{\Sigma P(dk)\cdot P(Sj/dk)},$$

where P(di/Sj) is the probability that there is a disease di in the presence of symptom complex Sj; P(di) is the probability of disorder di for a given /195 choice; P(Sj/di) is the probability of the presence of symptom complex Sj for disease di, which is known from medical experience; ΣP(dk)·P(Sj/dk) is the sum of the products of the probabilities of each considered disease multiplied by the probability of a given symptom complex for each disease.

Let us comment on this formula: P(di/Sj) is the unknown probability of disease for the given set of symptoms; P(Sj/dk) is the medical experience which has been acquired to the present time and is quantitatively expressed in the form of the probability of a given symptom complex for a given disorder. For example, the symptom complex for acute vascular insufficiency is more probable for a gunshot wound than for gout, and the symptom complex of "stomachache" is more probable for appendicitis than for hypertension. The probability of each symptom complex for any disease can be expressed by a number from 0 to 1.0. Although the textbooks and monographs do not yet contain accurate calculations of these probabilities, they may be expressed in the following manner: pathognomonic symptom complexes have a probability equal to 1.0, and frequently encountered symptom complexes have a probability equal to 0.7-0.9; the average frequency is 0.5-0.6; rarely encountered symptom complexes have a probability of 0.3-0.4; very rarely encountered symptom complexes have a probability of 0.1-0.2; 0 denotes that the symptom complex is never encountered for the given disorder. P(di) is the probability of a given disorder in a group of randomly selected patients; this group may be the contingent of a given hospital, a given region, or a given city. The reason for introducing the quantity P(di) into the diagnosis is that it is not constant and depends on geographical, seasonal, epidemiological and other factors which the physician must take into account when making his diagnosis.

Thus, for example, the following group of symptom complexes exists during an epidemic: headache, weakness, and increase in body temperature matches the diagnosis of influenza with a probability of 0.95-1.0; the same symptom complex in tropical countries, in the absence of epidemiological factors, has a high probability for the diagnosis of heat stroke and hyperthermia.

The sum of the products of probabilities of each considered disease, multiplied by the probability of the selected (investigated) symptom complex for each given disorder [ΣP(dk)•P(Sj/dk)], is a conditional quantity which indicates the comparative value of a given symptom complex for a given disorder in comparison with other disorders. It is essentially a pathognomonic index. The greater the difference between the denominator and the numerator, the less pathognomonic the symptom complex.

TABLE 11. EXAMPLE OF THE CALCULATION OF VALUES OF CONDITIONAL AND UNCONDITIONAL PROBABILITIES FOR MAKING A DIAGNOSIS (R. LEDLY AND L. LUSTED). /196

Symptom complexes	Disease Complexes							
	0	1	2	3	4	5	6	7
0	0	0	0	0	0	0	0	0
1	0	1.167	0.167	0	0.100	0	0	0
2	0	0	0.067	0	0	0	0	0
3	0	0	0.200	0	0	0	0	0
4	0	0.33	0.06	0	0.30	0	0.20	0
5	0	0.50	0.16	0.33	0.60	0	0.20	0.20
6	0	0	0.16	0	0	0	0.20	0
7	0	0	0.26	0.66	00	0	0.40	0.80
Disease complex	0	0.60	0.15	0.15	0.05	0.04	0	0

Let us examine Table 11 as an example.* The table contains conditional and unconditional probabilities for 7 symptom complexes and 7 diseases [R. Ledly and L. Lusted]. The data in Table 11 do not have a factual basis and are strictly for purposes of illustration. Let us assume that our patient has the symptom complex M_4(S-4), in which diseases No. 1-4 (D-1, D-2, D-4, D-6) are possible. By means of the Bayes formula, we find the values of P(di/Sj), i.e., the probabilities of each of the 4 diseases in the presence of symptom S-4.

$$P(D\text{-}1/S\text{-}4) = \frac{0.6\cdot 0.33}{0.60\cdot 333 + 0.15\cdot 0.067 + 0.05\cdot 0.3 + 0.005\cdot 0.2} = 0.855$$

$$P(D\text{-}2/S\text{-}4) = 0.044;\ P(D\text{-}4/S\text{-}4) = 0.067;\ P = (D\text{-}6/S\text{-}4) = 0.004$$

Thus, disease D-4 is the most probable.

Detailed investigations of probability information evaluations in computer diagnostics have been conducted by the Soviet scientist, M. L. Bykhovskiy. He has indicated that the logarithm of the relationship between the conditional and unconditional probabilities of a given disease may be employed as an information measure of a symptom [41]. The conditional probability is the probability of a given disease in the presence of a given symptom complex P(di/Sj), while the unconditional probability is the probability of a given disease for a random sampling P(di). After designating the information measure of a symptom as α, we obtain:

$$\alpha = \log \frac{P(di/Sj)}{P(di)}$$

M. L. Bykhovskiy has also pointed out that the amount of information contained /197 in a symptom complex Sj with respect to a disease di is equal to the amount of information contained in a disease di with respect to symptom Sj, i.e., $\alpha_{Sj\cdot di} = \alpha_{di\cdot Sj}$. The determination of an information measure for the absence of a given symptom complex for a given disorder was also important in his opinion:

$$\alpha_{di\cdot Sj} = \log \frac{1 - P(Sj/di)}{1 - P(Sj)}$$

Bykhovskiy and his associates [42] proposed a logic diagram for a diagnostic process. The method includes the sequential application of deterministic logic, probabilistic logic, and phase-interval logic. The algorithm of this system was also given in the form of a matrix (Table 12) in which the diseases (D) are plotted along the vertical and the symptom complexes (S) are plotted along the horizontal. The unconditional probabilities of each disease are indicated in the left column, while the conditional probabilities of the symptom complexes for given diseases P(Si/di) are indicated at the intersection of the vertical and horizontal lines. The note indicates the symptom sets for deterministic logic.

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*Translator's note: In Table 11, the value of 1.167 for (D-1, S-1) should perhaps be 0.167.

TABLE 12.

P(di)	S D	S_1	S_2	S_3	S_n	Note
P (D-1)	D-1				$P(S_n/D\text{-}1)$	(S_1, S_2, S_7)
P (D-2)	D-2		$P(S_2/D_2)$			(S_3, S_6, S_n)
P (D-n)	D-n		$P(S_2/S_n)$			

The logical diagnostic process consists of two stages: deterministic and probabilistic. A diagnosis with complete coincidence of the patient's set of symptoms with the given set of symptom complexes can be obtained as a result of the first stage. If this coincidence does not occur, diseases are selected which are possible for the given set of symptoms. These diseases are rated according to probabilistic logic. The probability of each disorder is rated and the diseases with the highest probability are selected. If the probability value is insufficient for making a diagnosis, the volume of information is increased (the incertainty, i.e., the entropy of the situation, is decreased) by means of additional diagnostic investigations, and the probabilities are again calculated.

c) Other Types of Algorithms /198

Phase-interval logic. M. L. Bykhovskiy [43] has worked out the problems of geometric representation of normal and pathological states in the form of sets of points in a phase space. The phase space is constructed on the basis of a coordinate system whose axes represent certain parameters of the organism under investigation. The individual areas of this space make up a group of states, some of them characterizing a healthy organism, and others indicating various disorders (Figure 64). The current state of each organism is determined by a point in the phase space. A set of points (O) which differs from the set of points that are characteristic for various pathological forms of disease is formed for all healthy organisms. Each set has a center (AC), which is the most typical case of the group under consideration. The greatest distance between points of a given set is called the diameter of the set (D).

By using the concepts of the phase space, we can reduce diagnostics to the determination of the membership of a given point which characterizes the state of the organism to a certain set whose area corresponds to a specific disease entity. The various areas of the sets overlap one another, however, and it is frequently very complicated to match up one point or another with a specific set.

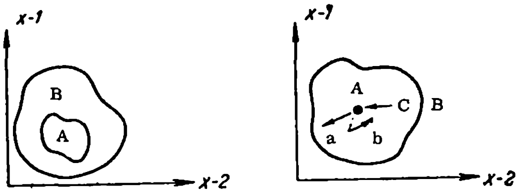

Figure 64. Phase-Interval Logic (See Text).

The diagnostic algorithm based on phase-space concepts is directed toward establishing the membership of a given point to the specific area. We must first know the center of the area which is closest to the investigated point. To do this, we calculate the so-called diagnostic radii, i.e., the distance from a given point to the centers of the various sets.

The criterion of the minimum sum of distances from a central point to all remaining points of a set or the criterion of the maximum product of these distances are recommended for determining the center of a set of points which characterizes the most typical point for the given disease entity.

A consideration of the dynamics of the development of pathological states from the standpoint of the phase-space idea is of definite interest. The set of points which characterize the various states of a patient over time form a certain trajectory of the development of a pathological process or its phase pattern. An organism which is left to itself as an autonomous system can: a) cross from a given area to another (improvement or aggravation of the symptoms); b) remain inside a given area (chronic case); or c) become equal to zero, /199
i.e., recovery. The last definition requires an explanation. It has been proposed [42] that the effectiveness of diagnostics with the application of the phase-interval method may be significantly increased if the deviations of the absolute values from the norm are selected as the parameters of the phase-space, rather than the absolute values themselves. Then the area of normal states is converted into a point, and the pathological areas approach the center of the coordinate system and narrow down, which makes it easier to find them. Thus, the transition to zero, or recovery, denotes the absence of a difference between parameters of a given organism and parameters which characterize a normal state.

The task of therapy consists of exerting actions on the organism in order to achieve a transition to zero on the shortest path. The phase trajectory can be corrected during the treatment process. It then becomes necessary to control a complex system with respect to the theory of dynamic programming.

It should be noted that the application of phase-interval logic should be preceded by matrix algorithms for excluding deterministic disorders. Probability algorithms also should be tried out earlier, since phase-space investigations are extremely complex and tedious from the mathematical point of view.

Algorithms which are based on the geometric interpretation of diagnostic information are not limited to phase-interval logic. Experiments on the construction of multidimensional hyperplanes established by equations associated with the probability characteristics of disease symptoms have yielded some very promising results. Attempts have been made to represent symptom complexes in the form of a multidimensional space [44].

Algorithms based on the search for a clinical precedent. One of the methods of evaluating diagnostic data which is employed in medical practice is to establish an identity betweeen the given case under investigation and other /200 known cases which have already been studied. A young physician always compares each new patient with the patients that he has already seen, or with abstract, idealized patients who precisely correspond to the descriptions contained in the textbooks. More experienced physicians, especially in complicated and vague cases, also employ association with other previously known cases. The search for a clinical precedent frequently renders invaluable aid to diagnosticians. However, the physician's memory cannot contain a full description of many cases. The physician can memorize only a few of the most interesting (complicated or atypical) patterns of clinical states. An automated search for a clinical precedent can suggest a great deal to the physician, help him to make a diagnosis, assist him in selecting a method for a complex operation, and provide aid in coping with possible complications [2].

The search for a clinical precedent is the sequential comparison of sets of symptoms which have been observed in specific patients with known disorders and with the symptom complexes existing in the given patient. Cases of coincidence are revealed as a result of research. However, one could hardly expect a complete coincidence. It is necessary to establish some variation limits for each symptom being compared (compulsory and noncompulsory symptoms). The medical archives from which the selection is made is a huge matrix in which each case history corresponds to a single-valued set of symptoms. The practical realization of a system which searches for clinical precedents was accomplished at the A. A. Vishnevskiy Institute [45] on the basis of punched cards. Each case history was represented in coded form. A corresponding number was punched in the card for each specific symptom existing in the patient.

The matching method is of interest not only for manifesting clinical cases which are analogous to a given case, but also for solving a number of scientific and practical problems. For example, this method makes it possible to rapidly detect the frequency of appearance of a particular symptom in a specific group of patients. Thus, S. Sh. Kharnas and his associates [46] give numerous examples of the solution to a number of diagnostic problems. In finding the frequency of coincidence of enlargement of the right ventricle (on the basis of x-ray data) with the presence of a dextrogram on an electrocardiogram, it turned out that of 420 patients, a coincidence was detected in 358, or in 85% of the cases. In the solution of the inverse problem, out of 454 patients with an enlarged right ventricle, a dextrogram was detected in 358, or in 78% of the cases.

The development of medical information systems to search for clinical pre- /201 cedents makes it possible to build up large libraries for subsequent statistical processing and to establish quantitative and probabilistic relationships between symptoms within specific disease entities. The absence of similar data at the present time essentially retards the construction of effective machine diagnostic programs.

The task of establishing medical libraries is closely related to the unification of case histories. A standard method for recording case histories in all clinics and hospitals of the country, which makes it possible to quickly transfer each case onto punched cards, would make it possible to rapidly acquire valuable materials for machine diagnostics and would provide for an effective search for clinical precedents on the scale of an entire city, region, or entire country. The task of setting up a centralized medical library for reference, diagnostic, and statistical purposes is an important applied problem of cybernetics.

Follow-up algorithms. As we know, the diagnostic process does not end with the making of a diagnosis, but continues during the course of therapeutic measures. The physician constantly rates the effect of his treatment, i.e., corrects his diagnosis in accordance with the change in the clinical picture. The automation of this process may foresee a set of matrices which correspond to the individual stages of a disease, so that the transition from one state to another can be identified with the transition from one set of symptoms to another. Practically speaking, however, the course of a disease in different patients is so individualized that the speed of disappearance of different symptoms and the degree of their expression fluctuates essentially. It is very difficult to combine sets of symptoms which correspond to the stages of development of a disease and the recovery of even a few patients in one matrix. Therefore, it is expedient to construct diagnostic algorithms for checking purposes under dynamic conditions on the basis of assigning an independent path to each symptom. We know that the changes in a number of indices during the development of myocardial infarct are different in various patients. Thus, normalization of a T wave can occur in the first week of a disease, as well as several months later. Restoration of the amplitude of ballistocardiogram I and J waves is observed in different cases on the third, fifteenth, and even thirtieth day of disease. The amplitude of ballistocardiogram waves often remains decreased even after clinical recovery. As we can see, it is practically impossible to devise a universal check program. One way out of this situation is to establish /202 thresholds for each index and to follow each one, if we also bear in mind the entire index complex. To do this, checkpoints are established, where the state of a patient corresponds to a definite set of symptoms.

Follow-up algorithms can be graphically interpreted as a dynamically variable (in multidimensional phase space) plane which is assigned by points with time coordinates, and an absolute quantity for each considered symptom. It is possible that this type of algorithm may be expressed by n-order differential equations. The realization of follow-up algorithms will obviously be more effective when used in conjunction with an analog computer, rather than a digital computer.

"Self-teaching" of diagnostic machines. Algorithms which do not require the application of electronic computers. One of the important properties of cybernetic systems is their self-teaching ability. New information arises in the process of self-teaching which is associated with a goal-directed search /203 for the most optimal operating conditions. A self-teaching cybernetic system with the appropriate selection of optimization criteria is capable of changing its own algorithms in the direction of the more rapid achievement of its given goal.

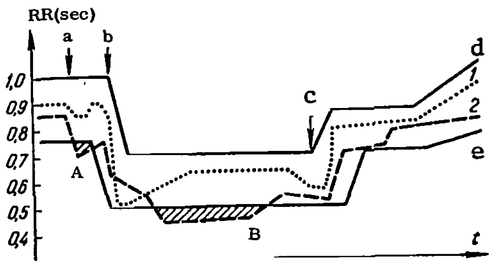

Figure 65. Follow-up Algorithm for Medical Monitoring during Physical Exercise. a = Preparatory Command; b = Beginning of Physical Exercise; c = End of Physical Exercise; d,e = End of Recovery Period: 1, 2 = Dynamics of Pulse Rate of Two Patients (Norm Range Bounded by Continuous Line); A and B = Pulse Rate Beyond Normal Limits; Algorithm Anticipates the Actuation of a Signaling Device at Moments of Time Corresponding to the Shaded Areas.

A "diagnostic machine" also can be used to improve diagnostic algorithms. The property of "self-teaching" makes it possible to automatically acquire experience in machine processing and data evaluation, and to consider diagnostic errors. In the event of an incorrect diagnosis, the machine makes corrections in its memory with regard to the thresholds of the values of individual indices or their probabilities, deviation combinations, etc. A self-teaching program is constructed in such a way as to reduce the number of erroneous diagnoses to a minimum. The self-teaching process can take place on the basis of library material and as a result of diagnostic work by means of direct data input from a human operator.

A self-teaching algorithm may be based on a series of trial diagnoses with various coefficients ascribed to each symptom. The coefficient is the weight of a symptom. The best set of coefficients will be found by comparing the machine diagnosis with the clinical diagnosis. The success of the self-teaching process depends on the number of analyzed cases. In essence, the machine changes its mind at a tremendous rate with each disease symptom fed into it and ultimately selects the one which coincides with a known decision. The speed of a mechanized self-teaching process is incomparably higher than the speed of human learning. Therefore, it is expedient to begin the acquisition of materials for machine processing with subsequent self-teaching as soon as possible. Successful algorithms for recognizing various diseases by means of the self-teaching of machines have already been worked out by many authors [41, 44, 47].

In addition to self-teaching, digital computers also make it possible to solve problems concerning the quantitative evaluation of symptoms in the general diagnostic pattern and to work out criteria which can be used subsequently in practice. Problems associated with the differential diagnosis of two similar diseases or disease forms are quite realistic. On the basis of the analysis of a certain number of cases, the machine can work out a sufficiently simple criterion (or group of criteria). Diagnostic Table 13 is given as an illustration of this proposition. The table is used to determine the probability of an extensive burn according to Ye. V. Gubler [48]. Wald's sequential analysis was employed when compiling this table. The data of 46 patients were processed and, /204
after working out diagnostic criteria, they were checked in 36 patients. The number of correct answers in the second case was higher than in the first. Diagnostic tables for differential diagnosis, compiled with the aid of a digital computer, can be used by physicians without special techniques. This will make it possible to increase the quality of diagnostics and will help to standardize the diagnostic methods and introduce mathematical methods in medicine.

TABLE 13. DETERMINATION OF THE PROBABILITY OF AN EXTENSIVE BURN OVER AN AREA GREATER THAN 20% OF THE BODY SURFACE.

pulse, number of beats per minute $\frac{90}{-133};\ \frac{90-120}{-5};\ \frac{120}{+77}$	immature leukocyte forms, % $\frac{0}{-29};\ \frac{0.5-1}{+12};\ \frac{1.5}{+27}$
total burn area, % $\frac{20-30}{-73};\ \frac{35-50}{+15};\ \frac{55-75}{+0.7};\ \frac{80-95}{+78}$	arterial pressure, minimum $\frac{50}{+77};\ \frac{50-90}{-16};\ \frac{90}{-48}$
morning temperature $\frac{36.5}{+54};\ \frac{(36.5-37.5)}{-0};\ \frac{37.5}{-77}$	leukocytosis, thous. $\frac{13}{-44};\ \frac{13-33}{-9};\ \frac{33}{+85}$
evening temperature $\frac{36.5}{+39};\ \frac{36.6-37.5}{+32};\ \frac{37.5-38.5}{-14};\ \frac{38.5}{-58}$	lymphocytosis, % $\frac{6}{+20};\ \frac{6-13}{-1};\ \frac{13}{-62}$
neutrophils, % $\frac{75}{-106};\ \frac{75-85.5}{-16};\ \frac{85.5}{+25}$	stab cells, % $\frac{5}{-45};\ \frac{5-14}{-17};\ \frac{14}{+28}$
arterial pressure, maximum $\frac{100}{+35};\ \frac{100-140}{-30};\ \frac{140}{+9}$	hemoglobin increase $\frac{2}{-50};\ \frac{2-4}{-27};\ \frac{4-7}{+20};\ \frac{7}{+0.6}$

The use of Table 13 consists of calculating the sum of the values in the denominator of the fractions, the numerator of which corresponds to the symptoms observed in the patient. The authors considered that if the sum of all values is greater than +127 (5% probability of error), there is an extensive burn. The answer is uncertain between values from (—127) to (+127); there is no extensive burn at values less than (—127). Upon further examination of this procedure /205 (table), we can see that we are essentially encoding the corresponding symptoms with the values "+", "n", "—" and are ascribing a weight to each sign, depending on the symptom. This is probabilistic-matrix logic and is accomplished without the aid of a computer.

It should be noted that the development of special diagnostic algorithms which do not require technical means is an important task. The work of S. N. Guiness is of interest in this connection. The existence of ordered and quantitatively expressed rules for accomplishing the diagnostic process can eliminate a large number of diagnostic errors if these algorithms are used extensively by physicians and are included in textbooks on diagnostics for students. Today, when diagnostics is based on the knowledge stored in the physician's memory and on the empirical approach to the evaluation of data with the most elementary logic operations, the introduction of standard diagnostic approaches is extremely important. Nonmachine algorithms can be worked out with the aid of digital computers and also as a result of the generalization of medical experience. Case history charts are essentially information collection algorithms. The charts of various laboratory investigations and special charts determine the data analysis algorithms to a certain extent; only information evaluation does not have concise algorithms at the present time.

Along with the necessity of the rapid introduction of computer technology, it is obviously necessary to utilize other possibilities of improving diagnostics: e.g., diagnostic tables. The development of diagnostic tables is the first step towards the introduction of mathematical methods in medical practice. After the appropriate testing, these tables may become the basis for differential-diagnostic programs of computers.

B. Some Questions on the Practical Application of Computer Technology in Medicine.

Ledly and Lusted [49] list the following diagnostic tasks which can be assigned to an electronic computer:

1) acquisition of a list of possible diagnoses which are compatible with the given set of symptoms;

2) determination of further diagnostic tests in order to obtain a differential diagnosis;

3) calculation of the probabilities of alternative diagnoses; /206

4) therapeutic recommendations;

5) compilation of statistical tables of the relationship between symptoms and diagnoses, and indications for the appropriate treatment;

6) performance of calculations for a qualitative interpretation of the results of complex diagnostic procedures (electroencephalography, phonocardiography);

7) retrieval of current information on new curatives and diagnostic methods;

8) storage and retrieval of necessary data on individual patients (case history, reaction characteristics).

G. Massari [50] indicates such possibilities of electronic computer technology as monitoring the therapeutic process, organizing statistical calculations in the clinic, hospital management, medical personnel administration and diet selection. There are other suggestions for the use of computer technology in medical practice. It should be mentioned, however, that a computer can do no more than follow its program, and the program is a reflection of the will and knowledge of the physician. Thus, a machine can never free the physician from diagnosis and therapy, nor will it even make his job easier. Computer technology can be used only to automate the elements of the physician's activity which yield to algorithmization, thus freeing the physician's mind and energy for creative work and for devising new diagnostic and therapeutic algorithms. A computer not only can replace a physician by following its prescribed program, but can also aid the physician in his creative research.

The extensive utilization of computer technology in medicine requires, above all, the standardization of data to be processed, as well as the standardization of algorithms and machine programs. ALGOL-60* is the most suitable for application as a universal language for diagnostic algorithms.

The algorythmic language, ALGOL-60, is distinguished by the fact that it uses elements of natural language, which facilitates the exchange of information between man and machine to a significant extent. The ALGOL-60 programming rules are quite simple and can be learned in a short time. There are special devices which automatically "translate" programs from ALGOL-60 into other "machine languages". /207 Algorithm standardization is extremely necessary for the exchange of algorithms between specialists. This will ultimately lead to the development of a single medical-information language which will provide for "free discourse" between physicians and computers, and will thereby make all the experience acquired by means of computers accessible to the physician.

The problem of establishing medical computer centers is closely related to the problems of standardizing the collection and processing of information. Such centers could perform a large number of tasks, including the rapid processing of collected information (electrocardiogram and electroencephalogram analysis), finding clinical precedents, providing "probable diagnoses", and giving advice with regard to treatment. Data input to the digital computers of this center could be organized, in addition to the conventional inputs with punched and magnetic tape, by way of telephone, with the possibility of obtaining rapid operational solutions. The establishment of specialized medical computer centers is economically more feasible than the use of individual digital computers in different clinics and, most of all, can provide a single approach to diagnostics and therapy and can accelerate the acquisition of experience (self-teaching algorithms). Let us examine some individual types of "diagnostic machines".

a) An Electronic Logic Device for Automatic Medical Monitoring

This type of "diagnostic machine" is distinguished by the rigidity of its operational program. A device developed by R. S. Dadashev, V. B. Malkin, and S. P. Khlebnikov [51], which automatically diagnoses hypoxia, will be considered below. The diagnosis is made on the basis of the continuous measurement of the main physiological parameters which characterize the state of an individual, extraction of the most informative signs, and recording of certain combinations of these signs (symptom complexes). The device is designed to send out five signals based on the number of various stages of hypoxia. The algorithm is represented in the form of a matrix, where the "diagnoses" are indicated along the vertical, and the input signals are indicated along the horizontal. There are five input signals. Each signal, depending on its value, is coded by the symbol 1, 2, 3, 4 or abs, which corresponds to the signs "+", "-", "n", and "p", which were considered above. Table 14 presents the values of the symbols for data /208 analysis, and Table 15 is a diagnosis matrix table for data evaluation*.

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*Abbreviation of ALGOrythmic Language. The number 60 indicates the year of publication of this language.

TABLE 14. SYMPTOM ANALYSIS

Symbols	A Intensity of bioelectrical activity of the brain in 2-8 Hz spectrum	B Heartbeat	C Oxygen saturation of arterial blood	D Respiration rate	E Arterial pressure
+p	⩾ 300%	⩾ 180%	> 65%		
n	⩾ 200%	⩾ 140%	⩽ 85%		
−p	⩾ 50%	⩾ 80%	-		
s		drop from 180% to 100% in 10 sec.	-		
—		< 40 per minute	< 60%	⩽ 2 per min	75% ⩽ Pmax
abs		200 per minute		⩾ 350 per min	⩾ 185%
+					

Note: s = special sign.

TABLE 15. DATA EVALUATION

	State of hypoxia	Symbols				
		A	B	C	D	E
1	stage of stable adaptation	n	n	n		
2	stage of partially uncompensated oxygen debt	+p	+p	+p		
2a	precollapse state	—	C	+p	—	abs
3	stage of completely uncompensated oxygen debt	—p	±p	+p		
3a	critical absolute values of physiological parameters		abs	abs	abs	abs

---

*These two tables are combined into one in reference [51], where the values are given together with the symbols.

A block diagram of the device is shown in Figure 66. It contains transducers (1), amplifiers (2), an informative-sign discrimination unit (3), converter units (4), and a logic unit and signaling circuit (5). A fronto-occipital /209 lead is used to record the bioelectrical activity of the brain. Respiration is recorded by a precordial transducer. Pulse rate is recorded by electrocardiogram. Oxygen saturation of the blood is determined by means of a transducer attached to an earlobe.

The informative-sign discrimination block and the converter blocks are equipped with indicator lights which signal not only the onset of individual stages of hypoxia, but also the achievement of a given threshold value in each channel. Thus, it is possible to continuously monitor the deviations of each informative sign from the norm and the approach of their threshold values by means of the indicator lights. The stages of hypoxia are indicated by means of multicolored signals. Arterial pressure is not measured continuously; it is measured only when the signals 2a and 3a appear.

b) The Digital Computer in a Medical-Monitoring System

This system is designed to perform operational medical monitoring in a clinic, operating room, physiological laboratory, gymnasium, and under various conditions which endanger health and life. One of the most complicated tasks is the selection of physiological parameters to be observed in medical monitoring. This selection is determined not only by the high information content of individual indices, but also by the reliability and simplicity of the information-collection system. Thus, for example, it is extremely desirable to record brain biopotentials when monitoring the state of the central nervous system.

A more or less stable electroencephalogram, however, is not possible when the test subject is in an active state. Consequently, a set of parameters which are not always optimum from the physician's point of view are optimum from the standpoint of the possibilities of technical achievement.

One of the important ways of designing effective automatic medical-monitoring systems with the use of digital computers consists in employing a limited set of physiological parameters which knowingly can be recorded reliably under the most diverse conditions, and as much information as possible can be obtained /210 on the basis of these parameters to achieve the necessary diagnostic effect (use of correlation interrelationships of physiological parameters).

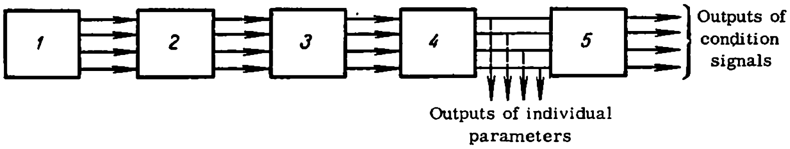

1
2
3
4
5
Outputs of condition signals
Outputs of individual parameters

Figure 66. Block Diagram of Electronic Logic Device for Automatic Diagnosis of Hypoxia [R. S. Dadashev, V. B. Malkin, and S. P. Khlebnikov, 1963].

An automatic medical-monitoring system with direct data input from a human operator to a digital computer was developed by R. M. Bayevskiy, K. K. Chernyshev, and V. A. Sharov [52]. It is based on the analysis and evaluation of four physiological parameters: electrocardiogram, seismocardiogram, pneumogram, and body-temperature data. The electrocardiogram ensures the acquisition of data on cardiac rhythm and the excitability and conductivity of the myocardium. Seismocardiography is the recording of the mechanical activity of the heart. A sensor is placed on the chest and vibrations associated with ventricular expulsion and filling are recorded. However, general body vibrations which considerably exceed the heart vibrations occur during motion. The seismo-sensor plays the role of a motor activity sensor in these cases. Respiration is recorded by a carbon sensor which reacts to variations in the circumference of the chest. Thermistors are used to measure body temperature. All sensors and electrodes are mounted on a chest harness and ensure obtaining high-quality information even under active conditions. The harness may be combined with a jacket or vest.

The digital computer-based system of automatic medical monitoring consists of the following units:

-- A physiological information-collection system;

-- A data-conversion system with input device;

-- A digital computer;

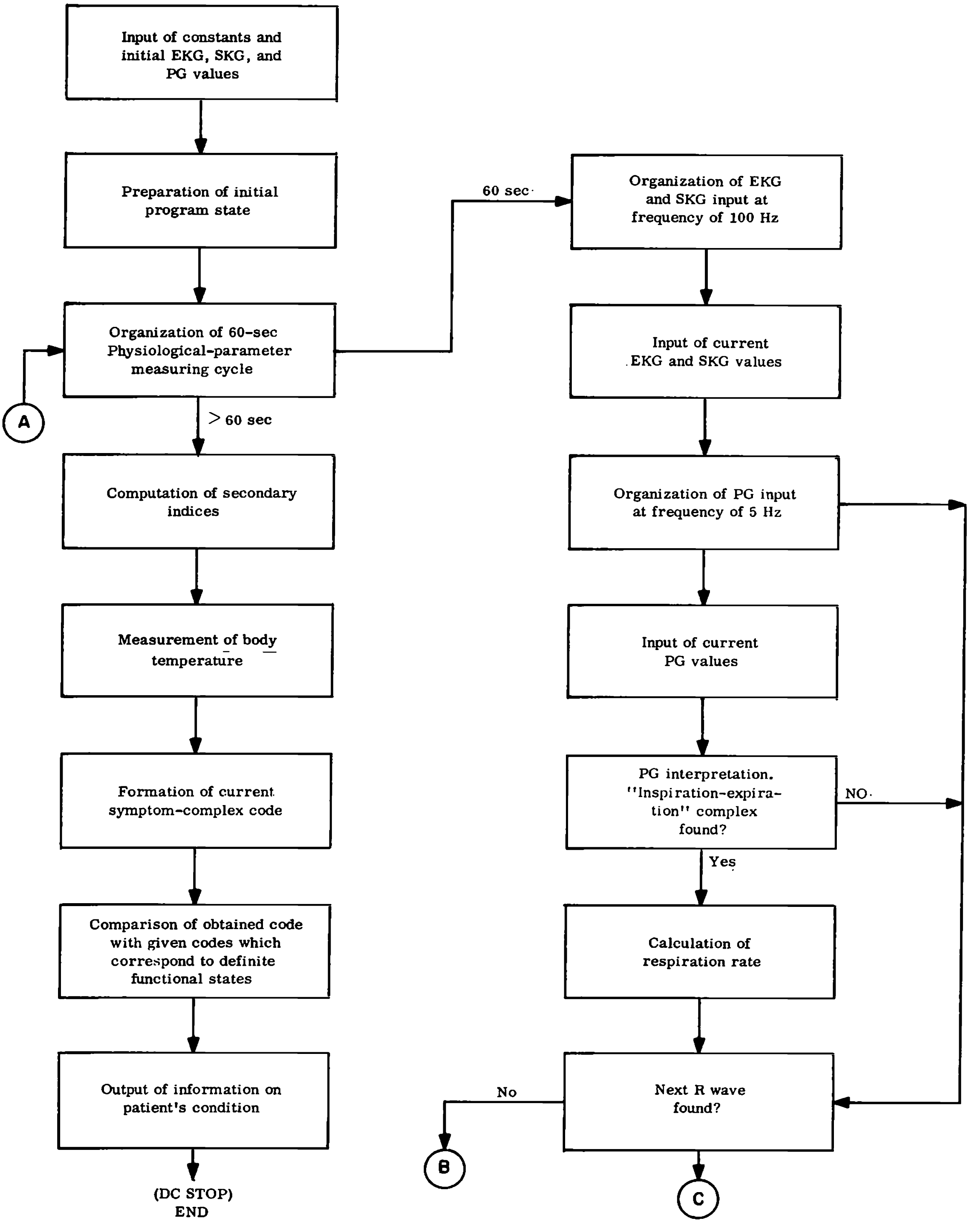
-- An output-data display system.

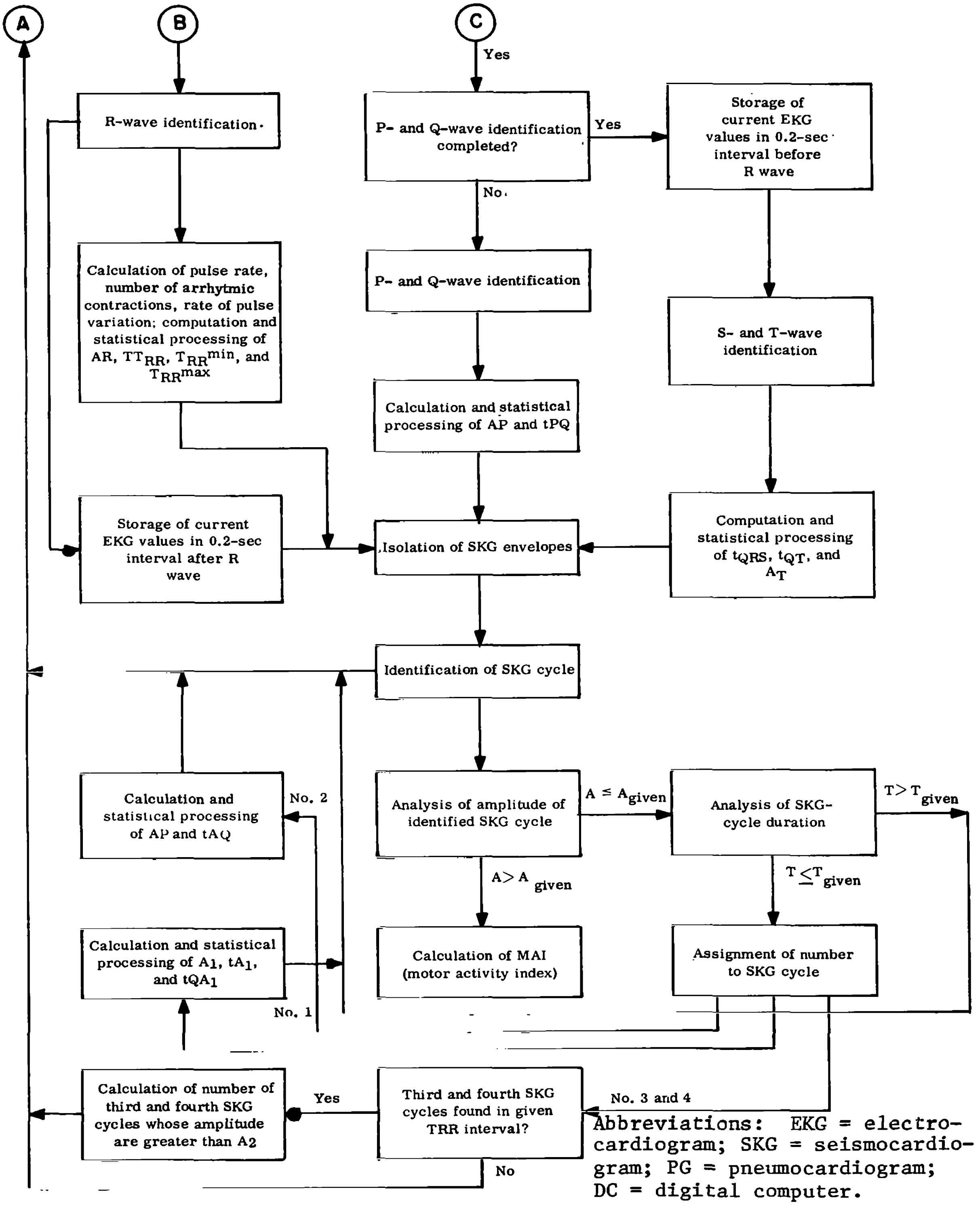
The questions related to the design of a physiological information-collection system were considered above. Data input is accomplished by an analog-digital converter which is directly connected to the outputs of amplifier equipment. /211 Any general-purpose digital computer may be used. When a single-address, fixed-point computer with a universal instruction system is used, the program and constant capacity amounts to 750 codes. An algorithm for automatic medical monitoring is shown in Figure 67. Table 16 gives the program for the solution of a medical monitoring problem (the program was compiled by V. A. Sharov and K. K. Chernyshev).

The algorithm and program require some explanation. The cyclic nature of the digital computer's operation should be noted. The measuring cycle continues for 60 seconds (this time can be varied). Data storage (statistical processing) and other operations occur in 60 seconds. One minute is the machine's time of inertness as a problem-solving device.

A response to a problem can be obtained in only 60 seconds. The selection of this particular length for the measuring cycle was prompted by the convenience of calculating pulse and respiration. Electrocardiogram and seismocardiogram input is accomplished at a quantization frequency of 100 Hz, and pneumogram input is accomplished at a frequency of 5 Hz. The current values of the parameters are analyzed. Characteristic points or elements are identified first. The R wave of the electrocardiogram is discerned by means of the following criteria (after signal differentiation):

TABLE 16. PROGRAM FOR SOLVING MEDICAL-MONITORING PROBLEM


Input of constants and initial EKG, SKG, and PG values
Preparation of initial program state
Organization of 60-sec Physiological-parameter measuring cycle
60 sec
> 60 sec
A
Computation of secondary indices
Measurement of body temperature
Formation of current symptom-complex code
Comparison of obtained code with given codes which correspond to definite functional states
Output of information on patient's condition
(DC STOP) END
Organization of EKG and SKG input at frequency of 100 Hz
Input of current EKG and SKG values
Organization of PG input at frequency of 5 Hz
Input of current PG values
PG interpretation. "Inspiration-expiration" complex found?
NO
Yes
Calculation of respiration rate
Next R wave found?
No
B
C


A
B
C
Yes
R-wave identification.
P- and Q-wave identification completed?
Yes
Storage of current EKG values in 0.2-sec interval before R wave
No.
Calculation of pulse rate, number of arrhytmic contractions, rate of pulse variation; computation and statistical processing of AR, TT_RR, T_RR^min, and T_RR^max
P- and Q-wave identification
S- and T-wave identification
Calculation and statistical processing of AP and tPQ
Storage of current EKG values in 0.2-sec interval after R wave
Isolation of SKG envelopes
Computation and statistical processing of t_QRS, t_QT, and A_T
Identification of SKG cycle
Calculation and statistical processing of AP and tAQ
No. 2
Analysis of amplitude of identified SKG cycle
A ≤ A_given
Analysis of SKG-cycle duration
T > T_given
A > A given
T ≤ T_given
Calculation and statistical processing of A1, tA1, and tQA1
Calculation of MAI (motor activity index)
Assignment of number to SKG cycle
No. 1
Calculation of number of third and fourth SKG cycles whose amplitude are greater than A2
Yes
Third and fourth SKG cycles found in given TRR interval?
No. 3 and 4
No

Abbreviations: EKG = electrocardiogram; SKG = seismocardiogram; PG = pneumocardiogram; DC = digital computer.

1) the leading-edge derivative of the R wave is positive and the absolute derivative is greater than the given value;

2) the duration of the R wave is from 0.02 to 0.06 second;

3) the trailing-edge derivative of the R wave is negative and the absolute derivative is greater than the given value.

This method makes it possible to reliably discern the R wave even when the isoelectric line is "floating" within ±40%.

The seismocardiogram is interpreted after preliminarily isolating the envelope.

The following 18 indices are measured during the measuring cycle:

PR = pulse rate;

Ar-PR = number of arrhythmic contractions (difference between adjacent intervals greater than 0.20 second);

PR_{max} = maximum difference between number of beats in adjacent 10-second time segments;

T_{RRmax} = maximum difference between duration of RR intervals in measuring cycle;

tQT_{av} = average duration of QT interval;

tTQ_{av} = average duration of PQ interval; /214

AP_{av}, AR_{av}, AT_{av} = average amplitude values of P, R, and T waves;

RR = respiration rate;

A_{1av}, A_{2av} = average values of amplitudes of first and second seismocardiogram cycles;

$tQAI_{av}$ = average interval between Q wave and beginning of first seismocardiogram cycle;

tA_{1av}, tA_{2av} = average values of duration of first and second seismocardiogram cycles;

$A_{3,4}$ = number of additional seismocardiogram cycles;

MA = motor activity (measured with seismo-sensor);

ST = skin temperature.

Thus, almost all of the indices are represented in the form of average quantities. The data obtained are analyzed with respect to four given values:

-- the upper and lower values of the norm;

-- the upper and lower values of optimum deviations from the norm.

The results are encoded as "+", "-", "n", and "p", and are then compared according to matrix logic.

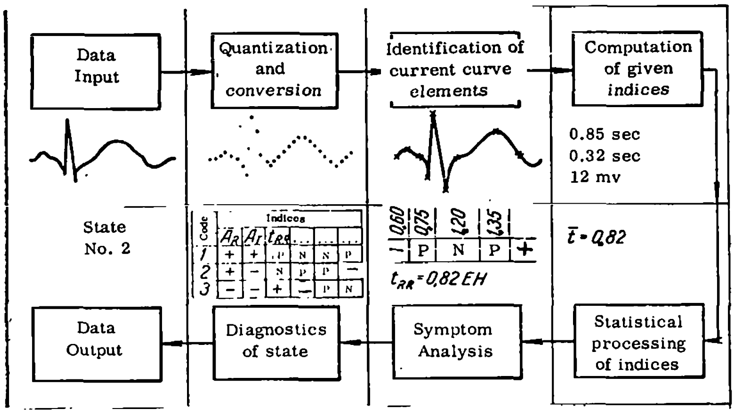


Figure 67. Algorithm for Automatic Medical-Monitoring System (see text).

In connection with the fact that the system employs a digital computer, it is quite simple to vary the optimum norm values for each sign, as well as combinations of deviations which characterize the /215 states of the subject, i.e., "the diagnosis". Thus, this system and its program may be adapted to solve the most diverse problems.

c) The Diagnostic System of the A. V. Vishnevskiy Institute of Surgery of the Soviet Academy of Medical Sciences

The diagnostic system of the A. V. Vishnevskiy Institute was designed mainly to diagnose congenital heart defects; however, the same principle can be used to design systems for diagnosing other disorders. The primary element of the system is the Ural-2 computer. Patients are examined by clinical physicians by means of various laboratory and instrument methods. The patient's symptoms are recorded on a special form which is fed into a digital computer either manually from a console or punched on a card [52]. A case history occupies 10 complete cells (40-bit) in the computer. The program of the diagnostic system consists of a medical memory and diagnostic logic. The medical memory is a table which consists of 50 diseases and 192 symptoms, and occupies 1200 cells. The medical memory can be improved by correcting the probability values of the symptoms. To do this, a card is specially punched in a certain zone and corrections are automatically fed into the machine memory.

The logic program (Figure 68, A and B) consists of the successive application of deterministic logic, probabilistic logic, and phase-interval logic.

The application if this diagnostic system has made it possible to obtain extremely good results. Thus, out of 125 patients with various congenital heart defects, the machine diagnosis coincided with the clinical diagnosis in 106 cases. A diagnosis was made in four cases as a result of the application of deterministic logic, while in 62 cases it was necessary to use probabilistic logic also [3].

d) Medical Diagnostic Centers

Cybernetics is opening up broad possibilities for automating the physician's work. We have already pointed out the help that a physician can receive from a computer when making a diagnosis. The possibilities of rapid processing /216 of large volumes of information and rapid analysis and evaluation of data with the use of algorithms which contain the experience of the most qualified representatives of medical science make it extremely necessary to widely introduce "diversified" diagnostic machines and devices for processing information. However, the installation of such equipment at every medical establishment, just as the generally employed equipment is now being installed (e.g., electrocardiographs), is economically impractical. In addition to the high cost of computer equipment, it must be maintained by experienced engineers and technicians.

Many authors have expressed the opinion concerning the desirability of establishing medical diagnostic centers which could serve the majority of clinics, hospitals, etc. [50, 54, 55].

We shall examine one of the possible projects for the creation of such a center. Its main tasks might be the following.

1. Processing and analysis of data from various instrument tests (electrocardiograms, electroencephalograms, etc.). /218

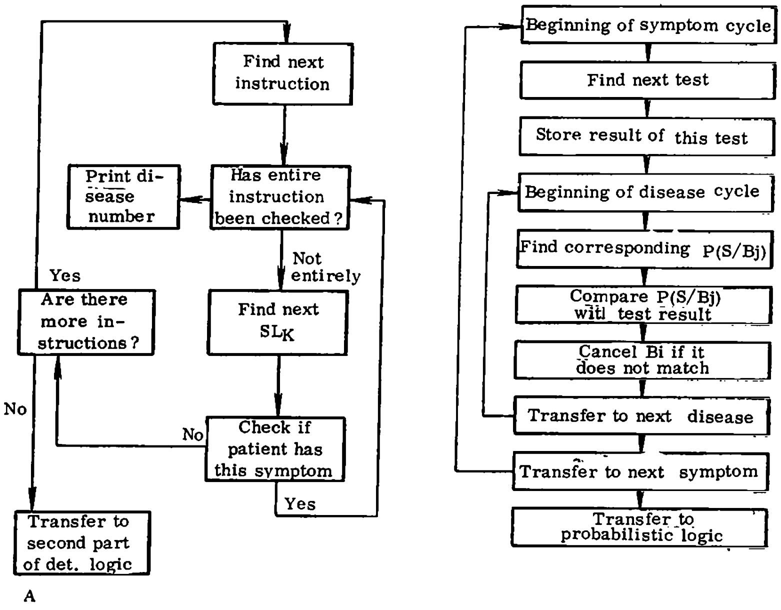

Find next instruction
Has entire instruction been checked ?
Print disease number
Not entirely
Yes
Are there more instructions ?
Find next SL_K
No
No
Check if patient has this symptom
Yes
Transfer to second part of det. logic
A
Beginning of symptom cycle
Find next test
Store result of this test
Beginning of disease cycle
Find corresponding P(S/Bj)
Compare P(S/Bj) with test result
Cancel Bi if it does not match
Transfer to next disease
Transfer to next symptom
Transfer to probabilistic logic

Figure 68. Block Diagrams of Diagnostic Programs for "Ural" Digital Computer Developed at the A. V. Vishnevskiy Institute of Surgery (by M. L. Bykhovskiy and A. I. Kurochkina). A = Deterministic Logic; B = Probabilistic Logic and Phase-Interval Logic.

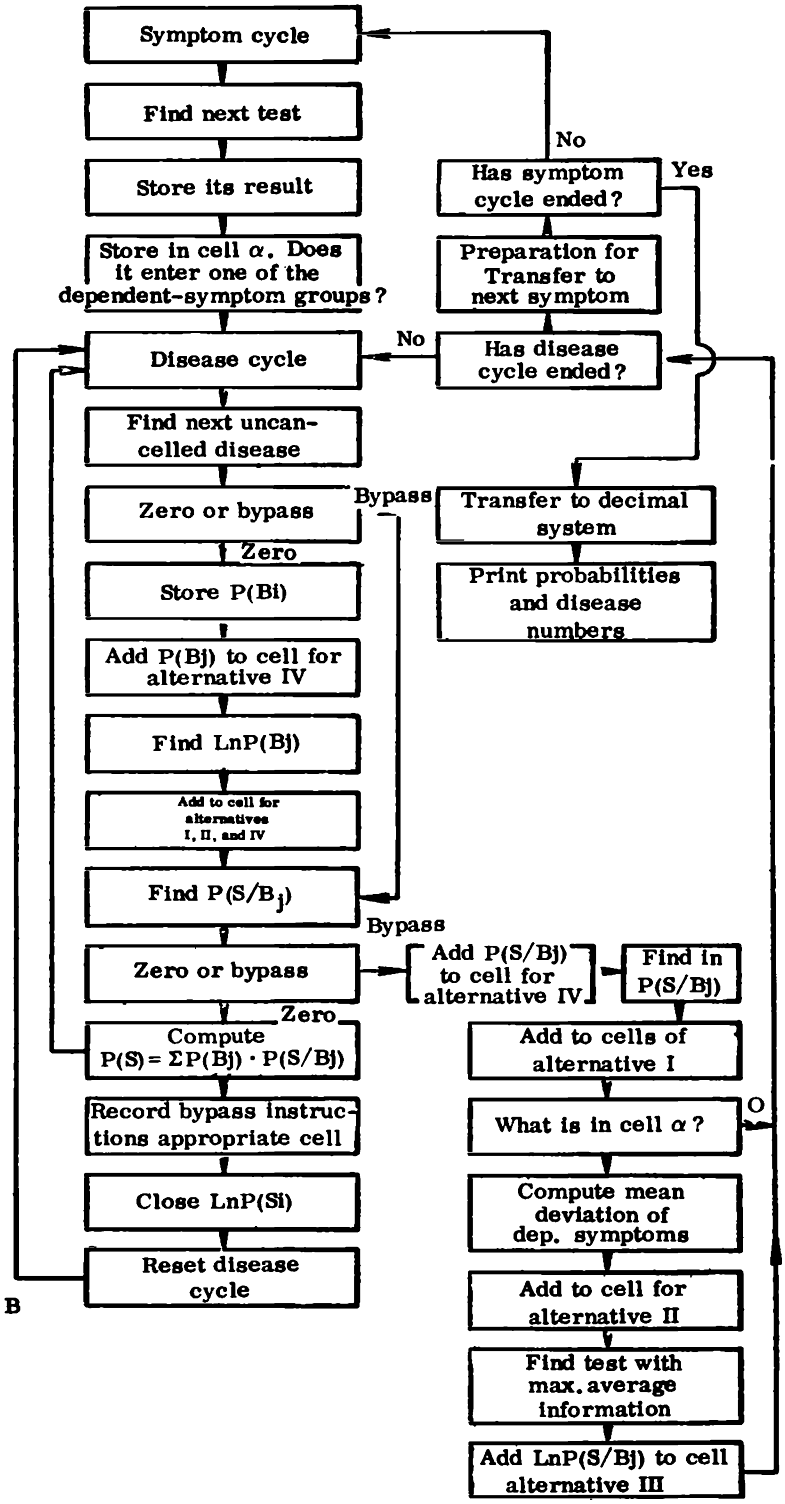

Symptom cycle
Find next test
Store its result
Store in cell α. Does it enter one of the dependent-symptom groups?
Disease cycle
Find next uncan-celled disease
Zero or bypass
Bypass
Zero
Store P(Bi)
Add P(Bj) to cell for alternative IV
Find LnP(Bj)
Add to cell for alternatives I, II, and IV
Find P(S/Bj)
Bypass
Zero or bypass
Zero
Compute P(S) = ΣP(Bj) · P(S/Bj)
Record bypass instructions appropriate cell
Close LnP(Si)
Reset disease cycle
B
No
Has symptom cycle ended?
Yes
Preparation for Transfer to next symptom
No
Has disease cycle ended?
Transfer to decimal system
Print probabilities and disease numbers
Add P(S/Bj) to cell for alternative IV
Find in P(S/Bj)
Add to cells of alternative I
What is in cell α?
O
Compute mean deviation of dep. symptoms
Add to cell for alternative II
Find test with max. average information
Add LnP(S/Bj) to cell alternative III

Figure 68 (Continued)

2. Assistance in making a diagnosis and selecting the treatment.

3. Storage of data on symptoms and treatment of various disorders for the purpose of establishing a medical library.

4. Automatic preventive examinations of large contingents of the population.

5. Centralized accounting for medical organizations.

6. Explanation of the dependence of morbidity rate on various meteorological, industrial, and socio-economical factors.

This list of tasks could be continued. We shall examine each task in greater detail, but shall first consider the probable structure of a similar diagnostic center. The main elements of the center, just as the main elements of the diagnostic systems described above, should be input and output devices, information storage and retrieval devices, and data-processing equipment. Data input, as we have indicated, requires the standardization of collection methods, the unification of recording methods, and the development of a single medical-language code. The diagnostic center should receive information on various carriers: e.g., punched cards, punched tape, magnetic tape, film, diagrams, etc. In addition, an important role may be played by direct data input by means of telegraph or telephone from a number of specially located hospitals and polyclinics. There might also be input key-punching from consoles located at the center itself.

Data output may be unified. A blank form with a printed text would be the most practical from our standpoint (there should be various types of blank forms for the solution of different problems). There must naturally be the possibility for remote transmission of solutions by telegraph or telephone. There should also be various output devices for seeing and hearing the data which are stored in the system's storage units.

There are presently units which can store up to 10^7 bits of information. It is expected in the near future that higher-capacity storage devices will be developed with sufficiently rapid information retrieval. The arsenal of storage devices now includes punched-tape, magnetic-tape, ferrite-core, magnetic-drum, and photo-optical models. The main difficulty in designing a storage unit for /219 a medical diagnostic center would not be its technical realization but the selection of an optimum method for encoding the data.

A modern computer with a speed of up to 100,000 operations per second could serve as the data-processing unit. These computers are now being serially manufactured, and the development of computers with speeds 10 and even 100 times greater can be expected in the very near future.

Figure 69 illustrates a possible block diagram of a medical diagnostic center. It may be assumed that such a center might be established preliminarily on the basis of a serial-manufactured digital computer (e.g., the "Ural" or "Minsk") with additional storage units and input units. It should be emphasized that the creation of a diagnostic center requires a great deal of research with regard to methods and procedures. Diagnostic algorithms must be selected, data input and output methods must be unified, standard forms must be designed, and a conditional medical code language must be developed.

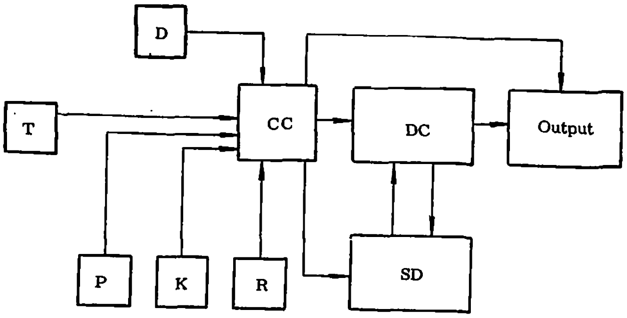


Figure 69. Proposed Block Diagram of Medical Diagnostic Center. D = Direct Data Input; T = Data Input by Telephone; P = Data Input from Punched Cards and Punched Tape; K = Input Key-Punching; R = Input from Tape Recorder; CC = Control Console; SD = Storage Unit; DC = Digital Computer; Output = Output Unit.

One of the most urgent problems of modern medicine is the timely and qualitative processing of recordings obtained from instrument examinations. The rapid growth of the number of diagnostic instruments in clinics and hospitals requires not only a corresponding increase in the number/220 of personnel (laboratory technicians in particular), but also makes the job of the physician significantly more difficult since he cannot examine and analyze each curve as he should. There has been an increase in the number of physicians who have detached themselves from purely therapeutic work and are occupied exclusively with the interpretation of instrument-examination data. A medical diagnostic center could automatically and rapidly process the recordings of hundreds and thousands of patients. The results of analysis can be given in numerical form, as well as in the form of final conclusions. Conclusions which could be obtained automatically with a single input of recordings from instrument examinations and the results of clinical examinations would be especially valuable.

There now exist some quite effective diagnostic algorithms which, in mass application, could be very useful. The mass utilization of machine diagnostics, however, also leads to accelerated self-teaching of the diagnostic system. This will make it possible to significantly improve the algorithms in time and, possibly, to raise the quality of diagnostics with a simultaneous increase in the volume of input data. This is an extremely promising path in the cybernetic development of diagnostics: i.e., the obtainment of a maximum of information from a minimum number of data. It is no secret that we are presently accumulating a mass of redundant information from the examination of patients which will never again be used. The examination of patients can be based on the use of cybernetics. The tremendous memory of a diagnostic system will make it possible to quickly find the appropriate clinical precedents, and a computer will make probability evaluations of different diagnosis alternatives and different modes of treatment. Computerized selection of the sequence of diagnostic procedures will also play an important role.

The high speed of the diagnostic system will create the prerequisites for conducting mass preventive examinations of the population and for creating an individual medical certificate for each citizen. This medical certificate will contain the main indices (physiological, biochemical, physical, etc.) which characterize the current state of health and will be compared with the results of the preceding examination, as well as with the standard growth characteristics contained in the memory of the diagnostic system prior to the next examination. The possibility has not been excluded that many preventive instrument /221 examinations will be conducted with direct data input to a computer.

The centralized processing of the work indices of all preventive-medicine organizations of a given region may be extremely essential for public health. A machine could quickly examine the distribution of patients in profile clinics, the dynamics of the morbidity-rate structure, the change in the needs of individual organizations for drugs, etc. In addition, these data, and also the data from preventive mass-scale examinations, when compared with the meteorological, industrial, and economical indices, will make it possible to raise the planning of public health measures to a high scientific level and to make rapid medical decisions which would affect the entire population.

The creation of medical diagnostic centers is quite realistic and feasible for modern medicine. There are rudiments of such centers today in Moscow, Leningrad, and Kiev in the form of diagnostic information systems at various clinics and institutes. A great deal of work must be done with regard to the organization of data input, the development of algorithms, and the standardization of documentation. The creation of medical diagnostic centers is economically the most expedient method of introducing computer technology in medicine. It is also the most progressive means of developing medicine, as it is in complete harmony with the principles of socialized medicine.

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Cybernetic Aspects of Medical Electronics

Medical electronics originated and became an independent scientific discipline in the last decade. Radioelectronic methods have been employed extensively in all fields of science and technology, including medicine. Individual electronic instruments and methods were used by only a small number of scientific laboratories and large clinics prior to World War II. Today, the electrocardiograph, x-ray equipment, diathermy apparatus, and other electronic instruments are present in practically every regional hospital and polyclinic. Electroencephalographs, electron microscopes, and photoelectric colorimeters have become instruments which are used daily by physicians. Electronic technology is being introduced into medical science and practice at a continually increasing rate.

A. I. Berg [1] distinguishes two trends of medical electronics: electrical and electrical-power. The instruments and methods for information collection and processing belong to electrometry. Electrical-power engineering includes all methods and instruments associated with the effect of energy on living matter.

The extensive use of electronics in medicine has made it possible to increase the accuracy of studying biological phenomena and has made a number of new, previously unknown processes accessible for investigation. It would not be an exaggeration to say that the origin and development of cybernetics is closely related to the achievements of medical electronics since the data on which Norbert Wiener's cybernetic concepts are based were obtained namely as a result of electrophysiological research. Along the same lines, as it frequently happens in the history of science, a young scientific discipline, i.e., cybernetics, which is scarcely on its feet, has begun to render a tremendous influence on the development of one of its parents, i.e., medical electronics.

What innovations will cybernetics make in medical electronics? An examination of this question is not only of scientific interest, but also has an important practical value; it will provide a better understanding of the main trends of modern medical electronic instrument design and will make it possible to determine its future prospects. The cybernetic approach to medical measurements compels us to consider any type of measurement from the standpoint of providing for the circulation of information in a system of interacting objects (e.g., the "patient-physician" system). The various instruments for collecting and recording data in this case (electroencephalographs, electrocardiographs) /228 are elements of a biological measurement and information system, which also includes a source of information and its recipient. This approach, which is reinforced by the study of algorithms for processing information in this complex system, creates the prerequisites for the subsequent automation of individual stages of the information process or even its complete automation (diagnostic machines). Secondly, cybernetics brings together the representatives of medicine and engineering, which affects the quality of new medical instruments and leads to new ideas in the field of medical instrument design. Thirdly, cybernetics is the basis for rearming medicine with new methods of collecting and processing information. We have in mind the extensive application of mathematics and digital computers. The utilization of new equipment and new capabilities requires further progress in the field of medical electronics. For example, it is necessary to develop storage and retrieval devices, various converters, etc. [2]. Finally, the area of application of medical electronics has been essentially broadened due to cybernetics. Research on psychophysiological processes [3], studies of the interactions in "man-machine" systems [4, 5] and the simulation of various biological phenomena [6] have been set up on the basis of instrument methods.

"Cybernetic" devices are presently only objects of research and development. Cybernetics and medical electronics will undoubtedly lift the fields of theoretical medicine and public health to a new level in the near future [7, 8].

Medical electronic instruments can be divided into three large groups.

1. Instruments for recording data from biological objects (directly or indirectly).

2. Instruments for generating information which is fed to a biological object or which acts upon its afferent systems (stimulants).

3. Instruments that convert information from a biological object into control signals which act upon the object or a technical device.

In spite of the fact that only instruments of the last group can be formally called cybernetic instruments, it can be pointed out that the first two groups of instruments also may be considered from the standpoint of cybernetics. If we /230 imagine that recording devices or stimulators are included in a "patient-physician" system as elements of an information-transmission channel, their characteristics should be considered with respect to the general task of functioning of the entire system. Thus, an electrocardiograph in a particular case, e.g., when performing complex surgery, is an indicator of disturbances (changes) in the state of the myocardium which are associated with surgical intervention. The surgeon receives information on the condition of the heart during the operation and appropriately changes his tactics if there are signs of acute coronary insufficiency, heart block, or extrasystole. Thus, the disturbances are regulated. The application of an electroencephalograph for monitoring the administration of an anesthetic can be considered in a similar manner.

Figure 70 illustrates generalized diagrams of various types of medical instruments from the standpoint of cybernetics. These diagrams not only illustrate a new concept (the cybernetic approach to problems of medical instrument design) but also indicate the possibilities of optimum designs of various medical electronic equipment to perform various tasks. Unfortunately, the operating conditions of many instruments have not been taken into account during their design until recently, and this has often led either to excessively complicated and expensive instruments, or to unjustified simplification. For example, from the standpoint of information theory, the transmission bands of all elements of a system should be matched with one another since it is useless to strive for very small measurement errors in one of the system's elements if the other elements introduce greater errors [9].

Therapeutic-Diagnostic Equipment

The development of electronics and cybernetics has made it possible to begin the design and implementation of a number of new instruments. The great possibilities of automatic diagnostics were pointed out in Chapter III. Automatic equipment for monitoring patients has been employed in other countries. One of these devices is designed to simultaneously monitor 25 patients. Electronic units are installed near the beds. These units are connected by cables to a central post, where the limits of safe values of the monitored parameters have been /231 programmed for each patient. When a parameter goes beyond its safe limits, a light goes on and a sound is heard. The following indices are monitored: pulse and respiration rate, body temperature, arterial pressure, and rate of fluid flow (e.g., drop methods) [10]. Two types of serial-manufactured monitors, the MA-65 and MD-65, have been described [11]. They make it possible to simultaneously monitor six patients and to record or observe the pulse and respiration rate, body temperature, and arterial pressure. It is interesting to note that these monitors employ information-collection methods which ensure long-term monitoring. Pulse rate is recorded by a photocell placed on a finger and respiration rate is recorded by a nasal thermistor. The patient's clothing is fitted with three thermistors to

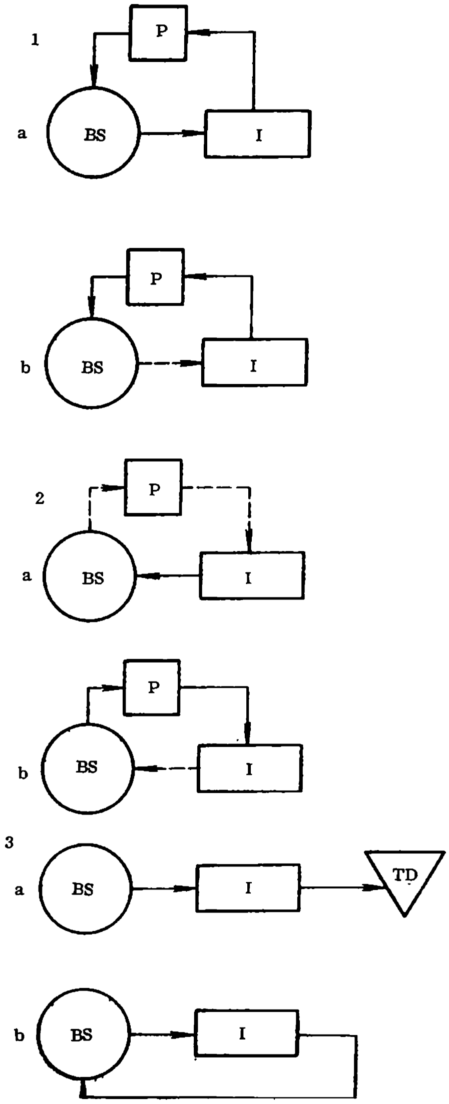

Figure 70. Medical Electronic Instruments from the Cybernetic Point of View. 1 = Recording Instruments; Electroencephalograph with Analyzer and Integrator (a); Automatic Erythrocyte Counter (b); 2 = Information Generators: Electrocardiostimulator (a) and Photophonostimulator (b); 3 = Instruments for Converting Biological Information into Control Signals: Phase Roentgenocardiograph (a) and Instrument for Controlling the Administration of an Anesthetic via Brain Biopotentials (b). BS = Biological Subject; I = Instrument; P = Physician; TD = Controlled Technical Device. Direct Communications Between Physician, Patient, and Instruments are Indicated by Solid Lines and Indirect Communications are Indicated by Dotted Lines.

measure temperature (the three thermistors reduce the time constant of the measuring circuit).

Questions regarding automatic monitoring of patients within an entire hospital [12] and also monitoring heart operations from one center [13] are being discussed. In addition to centralized measuring systems, cybernetic methods are being used extensively (with respect to automatic quantitative analysis) to develop new diagnostic instruments for extremely diverse purposes: for studying tremors [14], galvanic skin responses [15], arterial pressure [16], electromyograms [17], etc.

The application of 50- and 100-channel recording systems ("bioviewers")* developed in the Soviet Union by V. M. Anan'yev and M. N. Livanov open up new possibilities [18, 19]. Extremely interesting data have been obtained with these instruments on the dynamics of electrical phenomena in the cerebral cortex [20]. Successful experiments are being conducted with similar devices for studying the physiology and pathology of the heart [21].

Significant achievements have been made with regard to the development of instruments for studying and monitoring cardiac activity. The cardiocyclograph [22] and various types of cardiotachometers and intervalographs [23, 24] have already crossed the thresholds of scientific-research laboratories and are beginning to be employed in clinical practice. New cardiac monitors are being developed. The "Kardalarm" compares the length of the cardiac cycle with a standard. Each deviation from the standard is picked up by a memory unit. If the number of deviations in a certain time interval is higher then the given number, an alarm is actuated [25]. Another instrument, which was specially designed for monitoring the condition of patients with the Adams-Stokes syndrome, has a memory unit and a register unit. A binary counter is driven by /232 a 1-Hz generator and is continuously returned to zero by signals from the patient's heart. If the number of signals at the counter's output is greater than the given value, an alarm signal is actuated [26]. The "Ritm-1", which was described in the preceding chapter, is the same type of instrument [27].

Along with the improvement of diagnostics, cybernetics is coming into active play in therapy. Diagnostic information directly affects the treatment plan and plays an important role for correcting therapeutic measures during treatment. Feedback is especially important in therapy systems, where methods are employed which could cause dangerous shifts in the organism as a result of an incorrect dose of medicine, etc. This particularly refers to radiation therapy [28]. Many drugs also require careful monitoring when they are administered to critical patients since we are dealing with a "black box" problem in any case due to the impossibility of making a detailed analysis of the pharmacotherapeutic effect. The inputs (pharmacotherapy) and the output of the tem (therapeutic effect) have a probability relationship in this case. Questions of operational monitoring play a primary role in surgery. The surgeon must constantly receive information on the patient's condition and "make decisions" in accordance with the information that he obtains. Automation of patient monitoring during an operation, and also in the post-operative period, is an urgent task of modern medicine [29]. Automated systems for recording and displaying medical information to the surgeon in a form which is convenient for rapid perception are being developed. The work being done on the creation of controlled artificial-circulation machines also is of interest.

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*Translator's note: Known as "biovizor" (sing.) or "biovizory" (pl.) in the USSR.

The introduction of automatic instruments in therapy clinics is just as important. Here it is important to provide prolonged monitoring of patients who are confined to bed, as well as patients in dynamic situations. Biotelemetry plays a large role in the last case. Many biotelemetry systems have been described recently. These systems make it possible to monitor the condition of patients at long distances [30, 31] and have been used successfully in clinics [32].

Several simple systems for monitoring patients under stationary hospital conditions have been developed at the present time. These systems are based on the application of stock equipment: radio receivers, sound recorders, pulse tachometers, and electrocardiographs. The input units are sensors of simple /233 design or amplifier-transmitter units which can be manufactured by any radio shop. Figure 71 illustrates one of the possible block diagram of a monitoring system. The system is designed for visual or audio monitoring with a capability for long-term data recording on magnetic tape and immediate-access recording on a standard electrocardiograph. It is possible to transfer the data to paper tape while examining separate sections of the magnetic tape. The equipment, which is installed in a physician's office or at a nurse's post, includes a standard radio receiver (with an ultrashortwave range), a sound recorder, a portable vector-electrocardioscope (VEKS-1P), and a single-channel, ink-writing electrocardiograph (EKPS-Ch). The additional equipment includes a modulator, a decoder, and a commutator. Various types of input units make it possible to monitor various patients. Critical cases are observed by means of a seismo-sensor or a ballistocardiographic sensor built into the bed and hooked up to a sound recorder, vector cardioscope, or electrocardiograph. Patients who have left their beds and are taking their first steps within the ward can be monitored by means of inductive respiratory telemetry, whereby signals are received by a loop made up of 20-50 turns of wire placed along the walls of the ward. The audio frequency is the information carrier in this case (B. V. Panin). Patients who are permitted to take short walks within the wards are monitored by a simple telemetry system (transmitter power less than 10 milliwatts). The application of seismocardio-

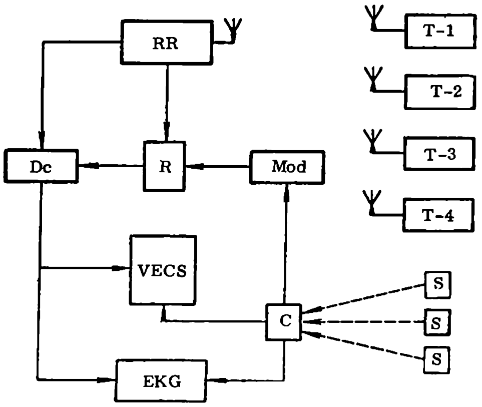

Figure 71. Block Diagram of Medical-Monitoring System which Utilizes Standard Equipment and Some Additional Devices. RR = Radio Receiver; R = Sound Recorder; VECS = Vectorcardioscope; EKG = Electrocardiograph; Mod = Modulator; Dc = Decoder; C = Commutator; S = Sensors; T = Transducers Worn by Patients.

graphic procedures is very convenient in these cases since the sensor does not require direct contact with the skin. Cardiac activity is recorded during rest /234 periods and actograms are recorded when the patient is active. Some important advantages of this system are: minimum expenses for equipment, the capability of monitoring various patients, and the possibility of prolonged data recording on a sound recorder with subsequent visual or audio examination of the information or even mechanical processing (with direct data input from magnetic tape into a digital computer.)

The introduction of methods of automatic diagnosis and therapy monitoring is of interest to many fields of practical medicine. Let us consider an example from the field of physical therapy (climatic treatment) in greater detail. Climatic therapy covers an enormous variety of physical factors of the weather, climate, and other therapeutic influences. There is also a large variety of disease manifestations related to sex, age, living and working conditions, etc. The physician's task is to correctly select a method of treatment, taking into account all of the conditions indicated above. In addition, he must appropriately monitor the condition of his patients during the treatment and make the necesssary adjustments, depending upon the effect to be obtained.

Thus, we encounter a typical "patient-physician" system, where one of the regulation loops is associated with the proper selection of treatment methods, and another loop provides continuous monitoring of therapeutic measures. Taking into account the complexity of individual proportioning and monitoring of therapy procedures under such conditions of mass therapy as exist at health resorts, several authors propose the use of cybernetic methods in these situations [33, 34].

Questions of algorythmization, and subsequently automation, in physical therapy and health-resort therapy* have an important value in increasing the effectiveness of socialized medicine. There is enough experience today to assist us in the selection of optimum treatment conditions in every case. This experience, however, has not been sufficiently generalized. The development of automatic devices to control the process of climatic treatment on a mass scale above all requires the construction of appropriate algorithms and the formulation of a list of input and output data. One of the first attempts to create a similar automatic device was made by Ye. G. Kesel'brener and his associates [34]. The automatic climatic-procedure dosimeter which they designed is an 11-kg semiconductor device with a data-output speed of 0.002 second. The first model had manual input of data on the patient and the environment; however, the authors are working on input automation. A block diagram of the automatic treatment- /235 procedure dosimeter is illustrated in Figure 72. Similar devices can be designed for different physical-therapy procedures not only at health resorts, but in clinics and polyclinics as well.

In addition, systems must be developed to monitor the state of patients at health resorts. This necessity arises from the fact that the physiological reactions of a diseased organism cannot be predicted precisely during treatment. We know of cases of the deterioration of a patient's condition even when the dosages had been very carefully selected. Operational medical monitoring might be useful in these cases. This type of monitoring would be based on a small number of criteria and would be actuated immediately following the completion of a procedure or while it is being performed. Such measurements as pulse and respiration rate and body temperature can easily be made by means of wires connected to patients who are receiving treatment, or even by employing radiotelemetry methods. Ballistocardiography procedures would be very suitable for monitoring on a beach since the mechanical effect of the heartbeat is very closely related to the level of metabolism, heat regulation, and neurohumoral regulatory mechanisms.

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*Translator's note: Soviet medicine has elevated the health resort to a scientific level and matters relating to the medical aspects of the health resort are covered by an independent discipline known as "Kurortologiya". The English translation could be "health-resort science" or "health-resort therapy".

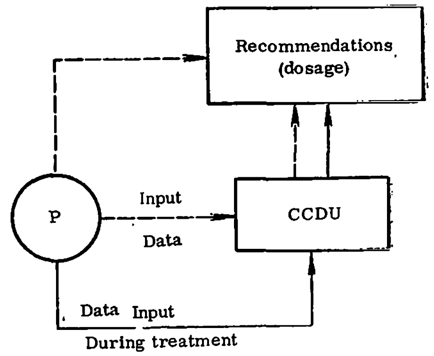

Figure 72. Automatic Treatment-Procedure Dosimetry (Ye. G. Kesel'brener et al., 1963). P = Patient; CCDU = Clinical-Climatological Dosimetry Unit.

Physical therapy and health-resort therapy, just as other medical sciences, are on the verge of extensively utilizing cybernetic methods. The development of cybernetic devices for therapy selection and monitoring is a task of the very near future. Controlled dosage methods will obviously be employed in the future. In this case the therapy process will be dynamically readjusted according to the current condition of the patient (dynamic programming methods). Biologically controlled systems will also have their place in therapy (conditioning of damaged muscle groups), as well as in the solution of medical-monitoring problems. Finally, we can expect some significant assistance from cybernetics /236 in automating the work of the support personnel at treatment centers.

Therapy may be considered as the process of actively influencing the control systems of an organism. When a physician administers drugs, he must precalculate the possible effect and select the optimum dosage. However, as we know, standard prescriptions and dosages are usually employed in medical practice; therefore, the treatment takes on the character of a random process and must be evaluated by the methods of probability theory, games theory, and the theory of random functions. We should also note the difficulty in obtaining a precise effect from drugs in connection with the individual sensitivity of patients to each drug. When physical therapy procedures are employed, electrotherapy in particular, the individual factor is taken into account to some extent, and the force of the effect (current, voltage) can be individually selected so that the desired reaction of the patient will be obtained. The effect is delayed in pharmocotherapy, which makes it difficult to regulate the therapeutic measures. In this case it is necessary to employ special diagnostic equipment to detect the reaction to a drug as early as possible. The establishment of feedback between a therapeutic action and the organism's reaction provides for an optimum therapy process and increases its effectiveness. Modern electronics is providing the physician with the technical means for detecting minimum shifts in the condition of organs and systems, while mathematical methods make it possible to extrapolate these shifts over time and to predict the possible effect in a number of cases. The ways and means of developing automatic therapeutic-diagnostic systems based on prediction and self-regulation are now becoming clear. No matter how fantastic these methods may seem today, the logic of the development of modern medicine provides us with a basis of think that such systems will be created in the very near future.

As an example, we shall point out the work done by K. D. Gruzdev and M. P. Spichenkov on the development of an automatic optimum-frequency stimulator [36]. The purpose of this work was to investigate the feasibility of automatic selection of the best form of therapy for a given patient at each given moment. The process of selecting the frequency of electrical stimuli was investigated.

The selection of an optimum frequency was achieved by controlling the feedback channel in such a way that the frequency of the stimuli was in a direct dependence upon the value of the signal at the input. The efficiency of the /237 stimulator was checked experimentally on a classical object, i.e., a neuromuscular specimen from a frog. Muscle biopotentials originated in response to rhythmic stimulation, and then acted upon the generator input by means of an amplifier. The frequency of the generator could be varied from 5 to 400 Hz. In the absence of a "feedback" signal (relaxed muscle), the frequency of the stimuli was 5 Hz. When the "stimulator-specimen" system is closed, muscle contraction leads to an increase in the frequency of stimulation. As a result of increasing the frequency of the stimuli, the muscle response reaches an optimum, and then enters a nonoptimum region with the further increase in frequency. A decrease in muscle response leads to a decrease in the frequency of impulses and the frequency is then stabilized in the optimum zone after several cycles of decreasing and increasing the frequency. Variation of the sensitivity of the feedback amplifier makes it possible to regulate the depth of feedback and, consequently, the automatic controllability of the system.

Electrical stimulators have been utilized extensively during the last few years in medicine and physiology. In principle, any action on an organism can be considered from the standpoint of information theory as the input of controlling information into the organism. The devices which generate controlling information can be designated as biological stimulators. Biological stimulators, thus, include drugs, climatic factors, and various types of physical action rendered on the organism. As we have already indicated, electrostimulators are the best with respect to controllability and individual dosage. It is not by chance that electrostimulators are beginning to be employed extensively in the most diverse fields of medicine. We might point out, for example, electrically induced sleep, electronarcosis, and others [37, 38, 39]. Methods of electrically stimulating the heart are very important in cardiology [40].

The effectiveness of the use of electrostimulation of the cardiac muscle is explained by the fact that the natural control information which constantly circulates in the heart also has an electrical nature. The first attempts at artificial electrostimulation of the heart to restore its functioning after death were made in 1802 by Aldini, a nephew of Galvani. He stimulated the heart of a decapitated criminal with an electrical current two hours after death; however, he was not able to stimulate a heartbeat. The first successful attempts at restoring the heartbeat in humans by means of electrostimulation were made by S. Gould (1929) and A. Hyman (1932). There are presently two types of elec- /238 trical heart stimulators: defibrillators for counteracting vascular fibrillation and rhythmic stimulators for artificially controlling the cardiac rhythm. Rhythmic stimulators have been developed for implantation in the chest. Figure 73, a and b, illustrates block diagrams of two types of electrostimulators which are implanted in the chest.

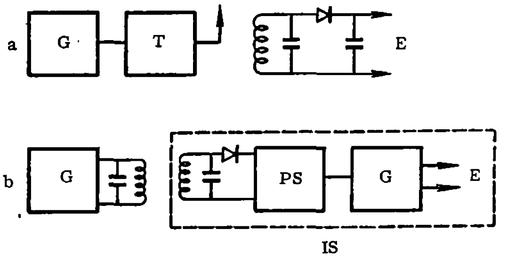

Figure 73. Block Diagrams of Two Types of Electrostimulators. a = Radio-Frequency; b = Self-Contained; G = Generator; T = Transmitter; PS = Power Supply; IS = Implanted Stimulator; E = Electrodes.

1. The radio-frequency electrostimulators are based on inductive coupling between the stimulator and the pulse generator. The pulse generator is placed outside the body and operates at a frequency of several MHz. The stimulator, which is implanted in the patient's body, is a plate with a diameter of 2.5 cm and a thickness of 0.5 cm. It is an oscillatory loop which is tuned to the frequency of the generator and connected across a diode detector to electrodes implanted in the cardiac muscle. The generator is situated near the patient and should have an output of 100-200 watts.

2. The self-contained stimulator is a flat disk with a diameter of 6 cm and a thickness of 2 cm. It contains a generator and a power supply. The generator provides pulses of 2-8 volts with a rhythm of 70 volts per minute. Power is fed to this generator from storage batteries which are designed for a service life of one week. The batteries are then given a boost charge across an inductive system similar to that of the radio-frequency stimulator.

Self-contained stimulators have been developed recently which provide continuous operation for three and even five years.

A great deal of work is being done in the Soviet Union on the introduction of electrostimulators into clinical practice and physiological research is being conducted in this area by Ye. B. Babskiy and his associates [40]. Devices which are similar to implanted cardiac stimulators are also being employed to stimulate other excitable formations; e.g., for prolonged controlled contactless stimulation of nerve trunks in long-term experiments with animals [41].

Questions regarding the controlled electrostimulation of various physiological systems of the body are being studied intensively at the present time. /239 The effectiveness of electrostimulation of the muscles in various disorders is well known. The action of an electrical current on muscle tissue in this case leads to the complex rearrangement of a large number of regulatory mechanisms associated with metabolism and hormonal systems. When the receptors of the uterocervical canal are electrically stimulated, positive shifts have been observed in patients with disturbances of the neurosomatic sphere which are based on disturbances in the activity of the gonads, particularly those associated with menopause [42]. We know of the value of electrostimulation of the urinary bladder in paralysis and electrostimulation of the respiratory muscles in poliomyelitis, for example [43]. Direct or indirect stimulation of the endocrine glands opens great possibilities for regulated actions on the body [44]. The work done by Delgado and his associates is of much interest. Their work was concerned with the remote stimulation of various portions of the cerebral cortex and subcortical centers in animals, including the use of remote-controlled pharmacologic actions on local portions of the brain [45, 46].

Electrostimulation as a particular case of biostimulation is of interest especially because of the convenience of control. In addition to special electrostimulators with broad capabilities in the area of action parameters [47], stimulators are being developed to act upon the visual and auditory organs (photophonostimulators), to control the dosage of x-ray therapy, to regulate oxygen therapy and, finally, devices are being designed to program the action of various physical-therapy and other measures by following instructions (e.g., from magnetic tape) which are given in accordance with the treatment plan established by the physician [48].

Automatic Instruments in the Laboratory and for Research

The introduction of cybernetics, automation, and electronics in medicine has led to the appearance of new instruments for performing clinical, bacteriological, and biochemical analyses. These instruments are characterized by automatic systems for collecting, interpreting, and analyzing information; they facilitate the work of medical laboratory personnel and increase the accuracy and effectiveness of patient examinations.

The development of automatic recognition theory provided the impetus for /240 the design of instruments to accomplish automatic recognition and subsequent analysis of various microscopic objects: e.g., leukocytes, erythrocytes, bacterial cells, etc. The operating principle of this sort of analyzer may be examined in an example of an instrument developed at the Institute of Biophysics of the Soviet Academy of Sciences [49]. An enlarged image of the specimen is scanned by a diaphragm whose size is significantly smaller than the size of the image. The luminous flux which passes through the diaphragm is converted by a photomultiplier into an electrical signal. The duration of the electrical impulses is proportional to the time of intersection of the object's image by the diaphragm. In the case of a round object (Figure 74), intersections occur along the chords and the electrical image of the object actuates a series of pulses of different length. To determine the dimensions of the particles, the pulse lengths are compared with given lengths and, as a result of calculation, a "remainder" is formed, which is also a measure of the object's area. Each subsequent and preceding line is compared to determine the number of particles. If the signals of these lines match, the object is still being scanned. If the signals do not match, the analysis of the given particle has terminated. A special counter is used to compute the number of particles. Checkout tests of /241 the counter have indicated a rate of computation (of erythrocytes, for example) of 200-300 particles per second, a computation error of ±2.8%, and a resolving power of 0.5 — 1μ. This micro-object analyzer has been used to count bacterial colonies, erythrocytes, leukocytes, and also to compute the distribution of

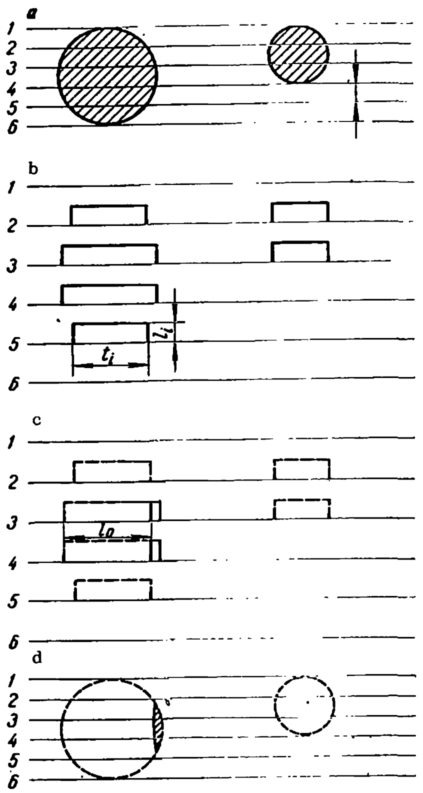

Figure 74. The Operating Principle of the Microparticle Analyzer. a = Depiction of Particles on Measuring Field; b = Video Pulses from Corresponding Chords (t_i = Pulse Duration, l_i = Chord Length); c = Comparison of Chord Lengths with Selected Value; d = Transformed Image of Particles.

micro-objects with respect to size [50]. The analyzer can be used to identify objects of a certain form from a complex set of objects on the basis of differences in size, optical density, or color. The analyzer has been used successfully for automatically counting and measuring brain cells [45]. Several other types of analyzers have been designed on the principle of image scanning [51, 52]. R. Bostom and his associates [53] described an instrument for automatically sorting cell smears for the early detection of cancer. Cervical smears were sorted. The purpose of the sorting is to select smears in which cancer cells were suspected during mass examinations. (Cancer cells have abnormally large and intensely colored nuclei). The time required to analyze one smear may be reduced to one minute, which makes the method suitable for organizing mass-scale preventive examinations. Scanning devices also make it possible to identify rarely encountered microscopic objects. For example, binuclear leukocytes are normally encountered in a ratio of no more than 1 out of 30,000, while their number may be essentially increased as a result of radiation damage. A special computerized system has been developed [54] which makes it possible to identify binuclear leukocytes. Identification is accomplished by means of space image quantization. The number of quantization operations is a measure of the size of a nucleus. Several automatic devices for counting formed elements in the blood are based on another principle. The instrument designed by A. I. Polivoda and described in L. F. Koblov's article [55] measures the electrical resistance in a capillary orifice through which there flows a isotonic solution that contains diluted blood. When a blood cell passes through the capillary orifice, the resistance changes sharply and an impulse appears at the output of the measuring circuit. A similar principle is used in the instrument designed by Douglas and his associates [56], who placed additional limitations on the amplitude of the impulses, which made it possible to distinguish particles with different diameters. A similar instrument is described by Cembranos [57].

Significant advances have been made in the automation of biochemical analyses [58, 59, 60]. Automatic nephelometers [61], automatic clotting-timers [62], and automatic multichannel devices for chemical analysis of various bio- /242 logical fluids [63] have been developed. The monograph, Automation in Clinical Chemistry, was published in the United States in 1963 [64]. The automation of laboratory investigations has left its mark in such areas as evaluating dilution curves in cardiology [65] and gastric juice analysis [66]. Figure 75 illustrates curves which were obtained as a result of automatic analysis of gastric juice in a healthy individual and in a patient with cancer of the stomach. Differences in composition of the protein fractions of the stomach contents are clearly noted.

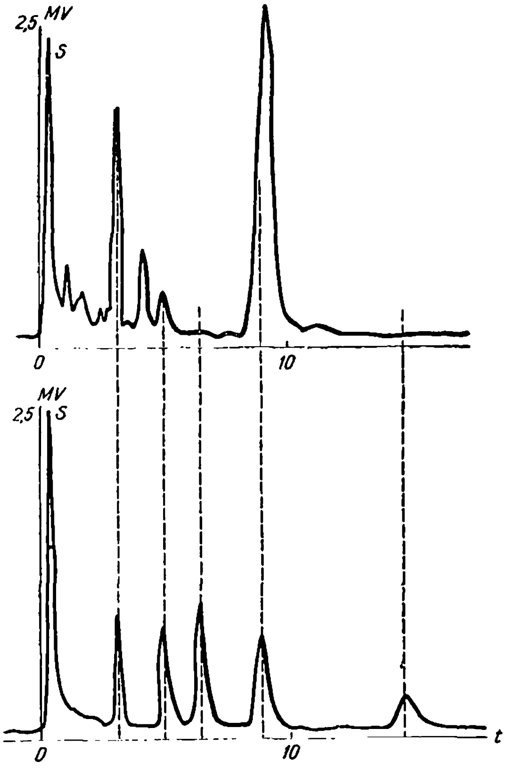

Figure 75. Automatic Analysis of Gastric Juice. Curves Obtained for a Healthy Subject (Top) and for a Diseased Subject (Bottom).

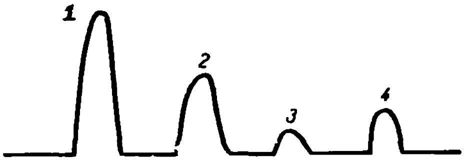

Figure 76. Mass Spectrum of Gas Mixture. 1 = Nitrogen; 2 = Oxygen; 3 = Argon; 4 = Carbon Dioxide.

As an example of an automatic gas analyzer, we shall describe a scanning mass-spectrometer for analyzing respiratory gases [67]. The instrument analyzes gases on a real time scale. A small portion of the analyzed gas /243 is driven through a capillary tube to decrease the gas pressure to 15 mm Hg. Positive ions are created in the ionization chamber as a result of electron collisions. The ions are focused onto a collector, depending upon the mass, at different accelerating voltages. Since the voltage varies (25 Hz), there occurs a pulsating ion current which corresponds to the mass spectrum of the given gas mixture (Figure 76).

Automation has also affected microbiology. Microbiological processes are characterized by the specific dynamics of culture development. Automatic multichannel devices for recording various indices during the cultivation of microorganisms take on an important value in connection with this fact. These indices may be the concentration of hydrogen ions, the oxidation-reduction potential, and temperature. The Institute of Microbiology of the Soviet Academy of Sciences has developed a device in which nephelometric measurements are made automatically in several culture containers over one measuring channel, whereupon the results of the measurements are inscribed on the paper tape of a recording instrument. A rotary mechanism with units that contain glass culture vessels is installed in a thermostatically controlled area of the device. The rotary mechanism revolves periodically at a certain angle and alternately places the vessels in a light beam between an illuminator and a photocell, which makes it possible to measure the light-transmission coefficient of culture fluid [68].

A great deal of material has been published recently concerning the automation of research work. Various programming devices for automatic stimulation have been widely employed [69]. For example, a special programmed device has been developed to investigate the motor reactions of fencers. This device, which works in conjunction with an electromyograph, has made it possible to conduct detailed analyses of the character of /244 motor responses during the performance of given types of movements (attack, defense) [70]. Programmed devices are being used in experiments with animals to study motor defense reflexes [71, 72].

As an example of the automation of some common experimental investigations, we shall describe a method for evaluating excitability thresholds of the neuromuscular apparatus in animals [73]. A laryngophone is used as a muscle-contraction indicator. It is attached to the body surface of the animal and connected across a transformer to an oscillograph. With a smooth increase in amplitude of the stimulating impulses by means of a miniature electric motor which revolves the potentiometer of a square-pulse generator, the resultant muscle contraction is recorded by the laryngophone. This procedure makes it possible to sharply reduce the variation in threshold values of electrostimulation of muscles and to increase the accuracy of the investigations.

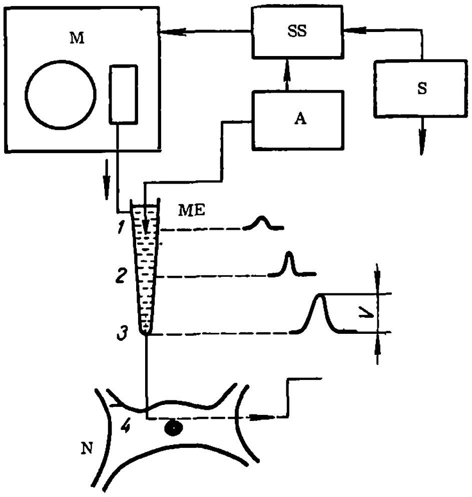

Figure 77. Servo System for Automatic Neuron Detection in Microelectrode Investigations (R. M. Meshcherskiy et al.). SS = Servo System; S = Stimulator; A = Amplifier; ME = Electrode; M = Reversing Mechanism; N = Neuron.

The servo system developed by R. M. /245 Meshcherskiy and S. R. Gutman [74] for automatic neuron detection during microelectrode investigations is of interest. A great deal of time is usually spent in searching for active neurons by means of step-by-step submerging of microelectrodes into the tissue. This procedure is tedious for the experimenter and involves the inevitable destruction of some neurons due to the fact that the experimenter cannot stop the advancement of the microelectrode in time. The device proposed by the authors operates in the following manner (Figure 77). When the microelectrode reaches point 1, extracellular potentials of small amplitude are reflected on a curve. As the microelectrode advances to point 2, the amplitude of the spikes increases, but does not reach the given threshold value V. The amplitude of the spikes reaches the threshold value at point 3, whereupon the microelectrode-advance mechanism is actuated. An R-C low-frequency filter is connected to the amplifier input to record intracellular potentials. This prevents the spikes from entering the control trigger. Only potentials with a duration of more than 100 msec and an amplitude of 30-50 mv can actuate the control trigger and stop the microelectrode (point 4 in Figure 77).

Biological Control

As the science of control and communication in the living organism and the machine, cybernetics is concerned not only with making analogies between engineering and biological systems, but also with the interrelationships between these systems. These questions were partially examined in the section "Man-Machine" of Chapter II, but there we discussed essentially human analysor systems, including the motor analysor. In the preceeding section of this chapter we mentioned the direct influence of control information on a living organism (biostimulation). These actions are associated with therapy problems and the object of control is a biological system. In this section we shall consider the possibility of utilizing biological information obtained directly from a living organism to control engineering systems.

The use of biological information for control purposes is very promising in various fields of engineering where human factors play a significant role. In particular, the problems of medical instrument design cannot be considered at the present time without taking into account the possibilities of applying the principles of biological control. One of the first biological control systems was the "artificial hand" invented by V. S. Gurfinkel', A. Ye. Kobrinskiy, A. Ya. Sysin, M. L. Tsetlin, and Ya. S. Yakobson [75]. This system was successfully demonstrated for the first time at the Brussels World Fair in 1958. /246

A slip ring for picking up muscle biopotentials was made in the form of a bracelet which contained metal cups filled with a current-conducting paste. The bracelet can be worn on the arm in such a fashion that the cups, similar to the electrodes employed in electrocardiogram recording, can be positioned at given points. The muscle biopotentials picked up by the bracelet are amplified by an electronic amplifier and fed to the input of a rectifier; the biopotentials are then sent to an integrating unit, where a control signal is formed; the power of the control signal is proportional to the value of the biocurrent power. The control signals act upon the coils of electric chokes which activate the artificial hand by means of hydraulic control. The difficulties in devising prostheses with bioelectrical control are primarily associated with the necessity of differentiating the useful signal from the interference [noise] caused by adjacent muscles. Another difficulty is brought about by the necessity of considering not only the biocurrents which originate in a muscle that directly performs a given operation, but also in antagonistic muscles.

There are two types of biological control systems: a) voluntary (mental) control systems, such as the "artificial hand"; b) involuntary control systems, where biocurrents of the heart, brain, respiration, and so forth [76] are used as control signals.

A biological control system consists of three parts: 1) an information collection unit; 2) a unit which converts the information into a form that is suitable for controlling effector mechanisms; 3) an effector mechanism (Figure 78).

The acquisition of control information from a biological object entails

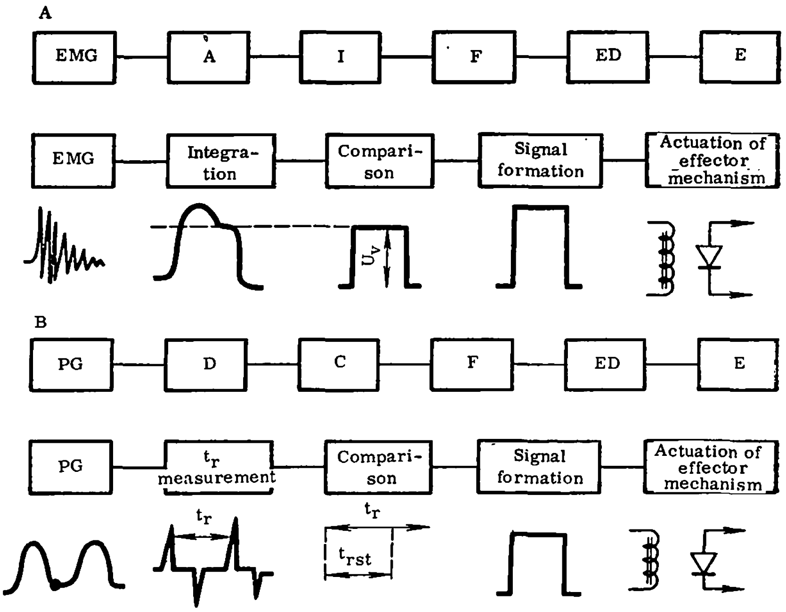

Figure 78. Block Diagrams of Voluntary (A) and Involuntary (B) Biological Control Systems. EMG = Electromyogram; PG = Pneumogram; A = Amplifier; I = Integrator; F = Filter; ED = Electrical Drive; E = Effector; D = Differentiator; C = Comparator; r = Duration of Respiratory Cycle.

some difficulty since an effective signal-to-noise ratio is necessary. For example, muscle-biopotential control requires the separation of signals of a specific muscle. The signal must have a specific power. Conversion into control signals is essentially the encoding of information. Depending upon the design of the effector mechanism, the control signals may have an analog or digital form. In some cases the effector requires only two positions: on and off. In /247 other cases there is a smooth change in the state of the effector mechanism with a linear dependence upon the control signal: for example, in a servo system. Other methods of effector control are employed in addition to the electrical drive. For example, in one model the problem of active prosthesis is solved in the following manner: muscle biocurrents are amplified and converted by a transistorized amplifier and control a valve which admits compressed gas (air or carbon dioxide) into an artificial muscle. The latter is a thin-walled rubber tube enclosed in a casing woven from thin steel wires. In the initial state, the fibers of this casing are arranged at a small angle to the longitudinal axis of the tube. This angle increases and the length of the entire system decreases under the influence of the gas which enters it under pressure.

Outstanding achievements have been made recently in the area of voluntary control by means of muscle biopotentials in connection with devising prostheses /248 for the upper extremities. Effective protheses with bioelectrical control have been developed in the Soviet Union. These prostheses are now being used by many individuals [77]. They are continually being improved. For example, a closed control system which employs feedback between an effector mechanism and man is being developed. Various types of sensitivity (e.g., vibrational sensitivity) are used in the feedback circuit for transmitting information to man on the actions which he is to perform. This will make it possible to accomplish strict proportioning of motor acts with respect to strength and coordination. A wrist prosthesis which was devised in Yugoslavia is of interest. Sensitive tensometer elements play the role of the tactile analysor and control a servo motor which performs a grasping motion [78]. Various logic and computer devices are now being used in the signal conversion unit [79, 80]. Various intensity "thresholds" of the signal are being used to obtain different commands. Several complicated motions can be performed from one command, whereby the prosthesis has "programs" for different motions. Bioelectric prosthetic control is one of the important practical achievements of applied cybernetics. The First International Symposium for Discussing the Requirements of Hand Prostheses, which was held in Yugoslavia in 1962, indicates the span of work being conducted in this area [82].

The use of muscle biopotentials for control purposes is of interest not only in prosthetics. Diverse remote-controlled manipulators or automatic protection systems can be designed on the basis of information received from muscles. Some American scientists have reported on the application of bioelectric muscle control in space medicine [83], 84]. Hand movements are difficult under high G conditions, which significantly lowers the effectiveness of spacecraft control. Devices are being developed to facilitate the pilot's hand movements. These devices are servo systems in which given movements of the extremities are performed by commands from muscle biopotentials. The research being conducted with robots controlled by the operator's muscle biopotentials is of interest. For example, the General Electric Company is working on a "walking machine" about 5 meters in height, which "repeats" all the motions of the man located inside it [85].

Voluntary biological control systems include systems which use the biopotentials generated during eye movements (electrooculogram) as control signals. /249 According to A. Lauringson, a 1° turn of the eye corresponds to a 10-40 microvolt change in electrical potentials. A linear dependence of the angle of revolution and the amplitude of the biopotentials is retained to 30°. It was pointed out that the tracking effectiveness in the "eye-brain-oculomotor muscles" system is better than in the "eye-brain-operator's hand" system [85].

Voluntary biological control systems also include the devices developed by French scientists for psychic (mental) control of engineering equipment by means of brain biopotentials. For example, a system was designed for control by means of turning on a light whenever the subject had a voluntary neuropsychic reaction [87].

Involuntary biological control may be based on signals which have an electrical character (bioelectric control), as well as on other types of signals. Instruments controlled by brain biopotentials were some of the first to be developed. In 1948, Prast and Noel [88] designed an instrument in which an increase in biopotential amplitude in a frequency range below 7 Hz actuated a warning device. In 1950, Bickford [89] invented a system in which the administration of ether to an animal during an operation was regulated by means of brain biopotentials. An electroencephalogram was subsequently used to actuate various warning devices by Malkin, Adamovich, Zilbertal, et al. [90]. A great deal of attention has been given to the development of automatic systems for regulating the administration of anesthestics [91, 92]; however, attempts to realize such systems on the basis of only one form of control information (brain biopotentials) have not been effective.

As we know, the clinical stages of anesthesia have definite electroencephalographic characteristics. By employing biocurrent analyzers, signals can be obtained for controlling the administration of anesthetics. This type of control system is based on the relatively simple relationship between the anesthetic concentration in the blood and the biocurrents of the brain. This system, however, does not take into account a number of factors which have serious implications during an operation and which determine the tactics of the surgeon and the anesthetist. We are bearing in mind such indices as the electrocardiogram, level of arterial pressure, degree of oxygen saturation of the blood, etc. The development of an improved system for controlling the administration of an anesthetic during an operation would require the simultaneous control of many /250 parameters. The number of controlling elements of the system must therefore be increased. In addition to varying the quantity of anesthetic being administered, the system would have to automatically control the administration of oxygen, the introduction of respiratory and cardiac stimulants, etc. The development of an automatic system which would control anesthesia in accordance with the given patient and the given operation without the intervention of a physician is realistically possible in terms of cybernetic principles. Changes in vitally important indices which occur during an operation will be picked up by special sensors and will regulate the different aspects of operating the anesthetic equipment by means of follow-up devices. These operations are presently regulated on the basis of a subjective evaluation of these changes by the anesthesiologist.

Individual elements of a future system for automatic regulation and monitoring of physiological functions during operations are already in existence. A paper on automatic regulation of arterial pressure was read by I. H. Green at the Third International Conference on Medical Electronics which was held in London in 1960. The operating principle of the instrument is based on the continuous reception of information on the arterial pressure of the patient by a follow-up device from an electromanometer [93]. A pressure drop below the given level starts a solenoid-actuated mechanized syringe which injects a specific dose of noradrenalin into the patient's vein. An excessive increase in pressure actuates a similar syringe, but this time filled with a hypotensive solution.

The variation in operating conditions of an artificial circulatory machine in accordance with the patient's condition can be automated by employing feedback regulation which indicates the level of arterial pressure and the extent of arterialization of the blood. The idea of developing a device for prolonged regulation of arterial pressure (e.g., in hypertonic patients, by means of a correcting device which operates in parallel with the natural regulators of arterial pressure and partially utilizes them) cannot be considered utopian today.

A great deal of attention has recently been given to biocontrolled systems which utilize respiratory information. A simple neonatal respiratory monitor was described in 1960 by Edge [94]. Biopotentials of the respiratory muscles /251
are being used to control artificial respiration instruments [95].

V. A. Tolyantsev proposed an interesting artificial-respiration control system [96]. He used the biocurrents of the phrenic nerve as control signals. These biocurrents are the output signals of the respiratory center and they reflect its functional state. This method of control is actually physiological and it maintains the respiration level in accordance with the organism's requirements. A similar system of electronic artificial-respiration control during open-chest surgery was developed by L. Montogomery and S. Stephenson, the only difference being that it did not utilize the biocurrents of the phrenic nerve, but biocurrents of respiratory muscles (alae nasi dilators)picked up by point electrodes. This instrument is equipped with a device which, independently of the biocurrents of the respiratory muscles, actuates rhythmic respiration if the number of impulses of the respiratory center drops below a certain predetermined frequency [97].

When examining the questions of biological control, it is also necessary to consider the use of heart biopotentials as control signals. In 1955, Jade and Gram [98] invented a device in which the QRS complex of an electrocardiogram controlled a stimulator with a given delay in the range of 30-3000 msec, which is necessary for investigating the conditions of the occurrence of extrasystoles in the hearts of mammals. V. S. Gurfinkel', M. L. Tsetlin, et al. [99] used the QRS complex to control an x-ray machine for tracing the heart in the different phases of the cardiac cycle.

The FRK-61 phase x-ray cardiograph, which was developed under the direction of I. K. Tabarovskiy, was subsequently mass-manufactured. A great deal of research and design work on the use of heart biopotentials for controlling various engineering equipment has been conducted by A. M. Medelyanovskiy and his associates. The materials of this work are presented in the collection *Phase Method of Studying and Controlling Functions of the Cardiovascular System* [100]. In addition to the control of x-ray equipment, heart biopotentials have been used for the following purposes:

-- phase study of cardiac excitability;

-- excision of part of the cardiac muscle in a given phase of the cardiac cycle, followed by biohistochemical and autoradiographic examination;

-- phase vector cardiography;

-- phase circulatory control;

-- actuation of cardiotherapy measures in a given phase of the respiratory /252
cycle.

The artificial ventricular-rhythm control system based on an electrocardiogram P wave is an interesting example of the use of heart biocurrents as control information. The first experiment on the application of atrial muscle biocurrents for controlling the work of the ventricles to create an artificial atrioventricular block was conducted by M. Folkmen and E. Watkins [101]. The potential of the atrium cordis was amplified to 500 mv by a transistorized amplifier with a gain factor of approximately 200 and fed to electrodes attached to the ventricular wall. The entire device, including the power supply, was placed on the back of a dog. A filter which did not admit frequencies above 130 per minute was installed to prevent tachycardia in the event of auricular fibrillation. Ye. B. Babskiy, G. Hellerstein [102], M. Kahn, and their associates [103] suggested that a time delay be placed on the pulses going from the atrium cordis to the ventricles, which is more physiological. Kahn and his colleagues used an instrument with an 0.15-second delay in clinical practice.

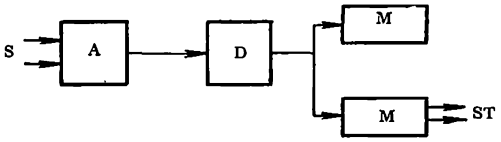

Figure 79. Electronic Bridge for Controlling Ventricular Rhythm by Means of the Auricular Potential (Kahn). S = Control Signal, Auricular Biopotentials; A = Amplifier; D = Time-Delay System; M = Pulse-Rate Monitor; ST = Stimulator.

Figure 79 illustrates the block diagram of an "electronic atrioventricular bridge". It should be noted that the electronic bridge is simultaneously a bioelectric control device and a biostimulator. The stimulus, i.e., the control *information*, is generated by the biological object itself, and not by an external device. This method is known as autostimulation. The systems mentioned above for regulating arterial pressure or the anesthesia device controlled by brain biopotentials are other examples of autostimulation. Consequently, autostimulators are devices which convert information on the organisms' condition into control signals.

In conclusion, to illustrate the broad possibilities of applying the principles of biological control in extremely diverse fields, we shall mention the sleep-warning system for vehicle operation which was patented in the United States in 1962 [104]. This system is based on measuring the electrical resistance of the skin surface of the palm. This resistance decreases sharply (by 3 times) when the body temperature is high, during sleep, or in a state of intoxication. Two electrodes are built into the steering wheel or other control device to measure skin resistance. An increase in resistance or a break in the measuring circuit first actuates a warning light and then an audio signal five seconds later. Similar devices may be useful in research work, in medical monitoring, and industrial safety. /253

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CHAPTER FIVE. BIONICS /261

What is Bionics?

The cybernetic approach to the consideration of the operating mechanisms of various living systems has resulted in the discovery of a number of new design principles for various engineering equipment. It is known that engineers frequently employ ideas in their technical projects which are already known to biologists. For example, prior to the development of the first radar equipment, biologists were familiar with the principle of ultrasonic ranging and detection used by bats. Since man is the most complex self-organizing system known in nature, there are undoubtedly many principles still unknown to science in this system which can be applied to engineering. The cybernetic approach to studying the human and animal organism provides many fruitful ideas for engineering. Another discipline with similar goals is bionics. Bionics is the application of the knowledge of biological processes and methods to the solution of engineering problems. Bionics is concerned with the study and development of engineering systems which have characteristics similar to the characteristics of living systems.

Bionics is a new engineering discipline based on the application of biological knowledge in engineering. It is not the same as biological electronics in which, conversely, engineering knowledge is employed to solve biological problems. The distinction between bionics and simulation also should be indicated. Research is the primary purpose of simulation. The main goal in bionics is the practical realization of the knowledge acquired by biology. The engineering devices created on the basis of achievements made in bionics, in turn, are models of living systems to a certain extent. They are practically useful models, however, as distinguished from the models used only to solve scientific [academic] problems.

Some authors distinguish three branches of bionics: biological, engineering, and theoretical [1]. Biological bionics is concerned with the study of living organisms for the purpose of explaining the principles which are the basis of the phenomena and processes that occur in the organism. This branch of bionics essentially includes any biological and physiological investigations which can be subsequently developed in an engineering aspect, i.e., can be used by engineers to develop new engineering concepts. Engineering bionics is a field of engineering in which new engineering systems and equipment are designed and old systems and equipment are improved on the basis of biological knowledge. Theoretical bionics is a branch of simulation which studies the feasi- /262 bility of creating an engineering device by pretesting a model of it (physical, mathematical, electrical, etc.).

The number of specialists who have shown an interest in bionics is exceptionally great. They include biologists and physiologists, physicists and chemists, radio engineers and shipbuilders. A specialist from any discipline may be called a bionicist if he is occupied with problems concerning the application of biological knowledge in engineering, It is obviously difficult to isolate individuals who are exclusively bionicists since there is no such specialty.

Each bionicist is a specialist in his field, a theoretician or practioner. The development of bionics is eliminating narrow specialization and bringing together various sciences to work on common problems.

The idea of applying the knowledge of living organisms for the solution of engineering problems was expressed 400 years ago by Leonardo da Vinci, who attempted the construction of an ornithopter, i.e., a flight vehicle with flapping wings such as birds have. The impetus for the development of modern bionics was provided by cybernetics. Indeed, the main concept of cybernetics regarding the unity of control systems in living organisms and machines is leading to studies on the feasibility of utilizing the more sophisticated principles of biological control in engineering. The official birth of bionics took place in Dayton, Ohio (U.S.A.) in September 1960 at the First Symposium on Bionics, where more than 600 representatives of large scientific organizations and leading firms participated. The official emblem of bionics was also adopted at this symposium: a scalpel and a soldering iron connected by an integral sign (Figure 80). This emblem can be interpreted in two ways: the scalpel as the symbol of biology, the soldering iron as the symbol of engineering, and the integral sign as the unification of these two disciplines; or the scalpel as the symbol of analysis and the soldering iron as the symbol of synthesis. The motto of bionics was also adopted at the symposium: "Living Prototypes are the Key to New Technology". Symposiums on bionics have been held regularly in the United States every fall since this time. There were several symposiums and conferences on bionics during 1962-1964 in the Soviet Union and this new field of science is developing successfully there at the present time.

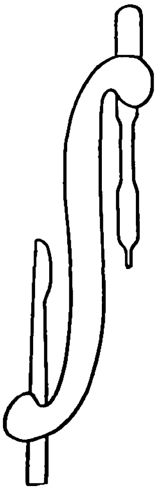

Figure 80. The Emblem of Bionics.

The progress of scientific research predominates today in bionics. Engineers and biologists are establishing areas in which the successful application of biological laws for the needs of engineering may be expected. New possibilities of fruitful cooperation between representatives of different branches of science are developing literally every day. Serious research is already being conducted in many areas [13, 14, 15]. /263

The first tendency was to consider bionics only in association with cybernetics, i.e., to study questions of employing methods of information storage, processing, and transmission in living organisms to design engineering systems. The range of interests of bionics in biology has now been extended from living information systems to the most diverse biological phenomena and processes. Many biological disciplines, including morphology and taxonomy, genetics and the study of evolution, have entered the sphere of attention of bionics. Thus, after emerging as a component part of cybernetics, bionics has quickly become a science which studies an extensive variety of functional and structural solutions of living matter.

The current research trends in bionics are associated with the following problems:

-- the study of the human and higher-animal nervous systems and the simulation of neurons and neuron networks for the purpose of further improving computer technology and for developing new components and units for automation and telemechanics; the study of the reliability of living systems;

-- the investigation of sense organs and other perception systems of living organisms for the purpose of developing new data sensors and detection systems; the study of recognition principles;

-- the study of the principles of orientation and navigation in various representatives of the animal kingdom in order to utilize these principles in engineering;

-- the investigation of the morphological, physiological, and other characteristics of living organisms to obtain new engineering and scientific ideas.

The range of these problems is being continuously expanded. As engineers enter the world of biological concepts, they manifest an interest in problems which would have scarcely attracted their attention previously. A confirmation of this fact is the extremely brief history of bionics, which began with the creation of artificial neurons, and is now extending its sphere of influence to such specific problems as increasing the speed of ships on the basis of studying the morphology of fishes.

Research on the Nervous System and the Problem of Reliability

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The human and higher-animal nervous systems are already inferior to computers in several aspects. The shortcomings of the nervous system from the engineer's point of view are its low speed (the psychophysiological process time is within the limits of 0.1 second), the impossibility of simultaneous reception of several different information flows, and the factors of fatigue and emotional instability. However, there are several qualities of the nervous system which give man an indisputable advantage over the most complex modern control systems and the latest cybernetic automata, and make man the most important and most reliable component of these systems. These qualities are the following:

1. Extremely sophisticated and flexible means of receiving external information. The contemporary cybernetic devices cannot pick up information in the form of handwritten or printed text, in the form of drawings, speech, moving images, etc.

2. High reliability, significantly exceeding the reliability of engineering systems. We know that engineering devices malfunction when just one component fails or when a circuit is broken. The reliability of components in engineering systems decreases as their quantity increases (there are several million components in computers). The nervous system of a living organism contains billions of nerve cells and the efficiency of the entire system is maintained even when several million of these cells are damaged.

3. The extremely small size of the elements of the nervous system. The

space occupied by the human brain amounts to approximately 1.5 dm^3 and contains approximately 10^{10} elements. A modern engineering device with the same number of elements would probably occupy a space of 10 x 10 x 100 m (the dimensions of a skyscraper).

4. The economy of the nervous system. The total amount of energy consumed by the brain does not exceed more than just a few watts, while an energy source equal to the power of the Dnepr Hydroelectric Power Plant would be required to supply 10^{10} transistorized flip-flops (each flip-flop represents one neuron).

5. The high degree of self-organization of the nervous system and the rapid adaptation to new situations and changes in the programs of its behavior. Most of the contemporary cybernetic systems follow rigid, predetermined programs. The simplest self-organizing systems have strictly determined functions /265 and specific purposes.

If we were to consider the processes of thought, memory, and consciousness, the list of the so-called advantages of the brain could be continued; however, it is quite clear that engineering can learn a great deal from nature. It is natural that the first attempts to simulate the human and animal nervous systems began with the development of neuron and neuron-network analogs.

The neuron, in its contemporary definition, is the main structural element of the nervous system. Certain simplifications have been made when devising neuron models. The formal neuron models that have been constructed at the present time are computer elements with the following properties.

1. The circuit of the neuron model has several inputs and one output. Each input and output can have only two states: ON and OFF.

2. The input signals act upon the neuron across contacts in which the arriving signal is delayed for a certain length of time.

3. The neuron is excited as a result of feeding it stimulating and inhibiting signals, while the neuron model is actuated only if the sum of the arriving signals exceeds a certain threshold.

There are other conditions which determine the operation of artificial /266 neurons, but it is not necessary to discuss them in detail here. Figure 81 illustrates a schematic representation of a neuron, while Figure 81a shows a neuron model and a circuit diagram of an artificial transistorized neuron.

Various types of artificial neurons have been developed: e.g., neuromimes, arthrons, neuristors, and others.

Neuromimes. The main type of neuromime is a converter with a dual output and two kinds of inputs: stimulation and inhibition. Designers are trying to obtain and are obtaining neuron analogs which possess a number of properties of natural neurons, i.e., not only with stimulating and inhibiting impulses on the inputs, but also actuated by the arrival of a certain threshold value of energy built up in a certain length of time, a recovery period which consists of the time of absolute and relative insusceptibility, a capability /267 for time and space summation, an output pulse of constant magnitude and duration, etc.

The design of one of the first neuron analogs, which was developed at the Rockefeller Institute, employed a device which simulated the presence of a membrane potential, sodium-ion conductivity, and polarization. A more complex neuron analog was developed at the Applied Physics Laboratory of Johns Hopkins University in Baltimore on the basis of a slave multivibrator. The Bell Telephone Laboratories and the General Electric Company have also designed neuromime models. The

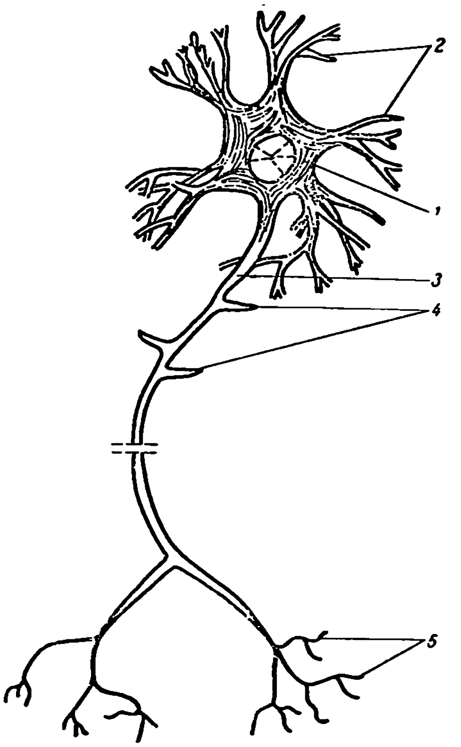

Figure 81. Schematic Representation of a Neuron. 1 = Body of Cell; 2 = Dendrites; 3 = Axon; 4 = Collaterals; 5 = Terminal Branch of Axon.

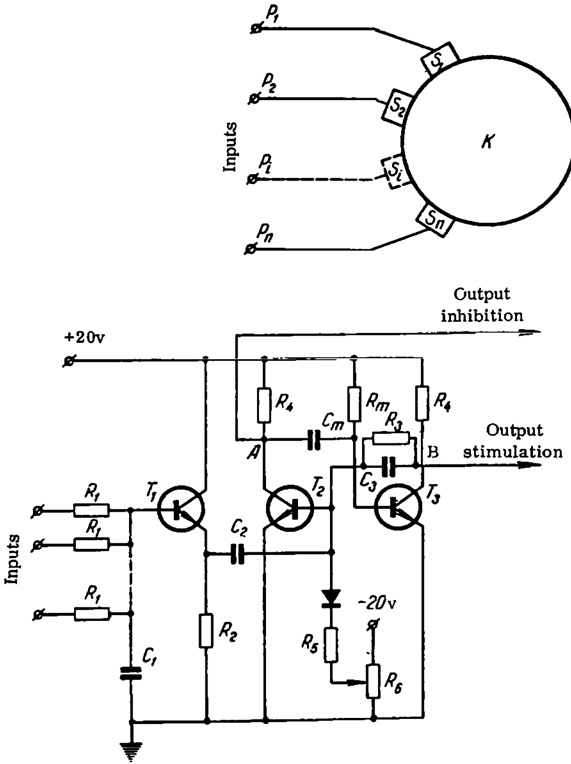

Figure 81a. Artificial Neuron (L. P. Krayzmer). Top: Neuron Model (Schematic Representation); Bottom: Circuit Diagram of Neuron Model.

latest model possesses the property of adaptation and has ten stimulating inputs and ten inhibiting inputs. The circuit of each stimulating input is equipped with a multiplier and a memory cell [2].

Arthrons. One type of neuron analog, which is called an arthron, is the basis for a self-organizing "thinking" machine which is currently being developed. The arthron has two inputs: "encouraging" and "punishing". Its logic functions act in one direction: from the inputs, which correspond to the dendrites, to the output channel, which simulates the axon. An arthron may have six possible states. The thinking machine is assembled from many arthrons connected together with direct communication and feedback. In the initial state, all arthrons (as well as the entire machine) are nonspecialized. The machine's tasks are determined and a criterion is established for adaptation to extensive changes in the environment while the machine is being "taught". A feedback circuit allows for errors in the "teaching" process. The combination of a logic operation with its encouragement or reproach determines the operating conditions of a noise generator, which permits or suppresses the given operation. As a result of the selective execution of an encouraged operation, the arthrons become specialized, and the entire system becomes organized: a change in the environment causes a transition to other logic operations.

The operational character of this machine is similar of that of an environmentally programmed self-contained system.

Neuristors. The so-called neuristor is another type of bionic element. It is an active instrument with distributed parameters and is made from strips of thermistor material and a distributive capacitor which runs parallel to it and functions as an energy accumulator. The neuristor is fed by a current which creates a uniform potential along the entire length of the instrument. When a certain portion of the neuristor transfers to an active state, energy is released in this portion, which causes local heating of the thermistor material. /268 This heating excites the adjacent sections of the channel, which continue to transmit excitation. A discharge is propagated in the same manner as in an axon, i.e., with uniform velocity and no decrement. Before the discharged portion can again enter an active state, energy must be built up in it (the capacitor must be charged), i.e., there occurs a period of recovery which corresponds to the refractor period of nerve fiber. This property further amplifies the similarity between the neuristor and the nerve fiber, i.e., the two waves, going towards one another, fade out.

If the neuristor is made in the form of a closed circuit with a length greater than the length of the recovery area, a given impulse will circulate infinitely. This effect can then be used for storage and rhythmic transmission of the impulse to other components of the neuristors.

An advantage of the neuristor system is its structural uniformity, which is defined as the uniformity of the distributed active-passive structure of its component elements, i.e., the fusion of the instrument and its connecting wires, as well as the possibility of direct connection of these elements into a complex circuit without the application of passive conductors. This system is also uniform from the functional point of view. All elements operate according to one principle, the signals are expressed by impusles, and there are no converters.

A device has been assembled on the basis of elements with neuristor characteristics. It duplicates the processes of memorization, recognition, and learning. A similar model was employed in W. Taylor's machine which, after exposing it to various objects, e.g., letters, recognized them in a repeated demonstration [3].

Another device was assembled on the basis of neuristor devices, the MIND (Magnetic Integrator Neuron Duplicator), which successfully performs the logic function of recognizing numerous variations of input patterns composed from several information signals [4].

The work being done on the creation of artificial nerve networks composed of model neurons with extremely diverse properties is of importance. The various aspects of cerebral activity are being studied by means of artificial nerve networks: e.g., memory, signal separation against a noise background, logic operations, the learning process, etc. In addition to physical networks composed of neuron-like elements, nerve networks are being simulated with the aid of computers and are being synthesized mathematically.

Let us examine a simple nerve network. Several model neurons form a nerve network. Each neuron has a body and an end plate which is in contact with the /269 body of the adjacent neuron. The end plates of several other neurons can be in contact with the body of one neuron. The end plates can be stimulating and inhibiting. The minimum difference between the number of stimulating and inhibiting end plates which leads to neuron stimulation is called the neuron threshold. For example, neuron A (Figure 82) is stimulated only if two stimulating end plates and one inhibiting end plate or three stimulating and two inhibiting end plates are simultaneously stimulated.

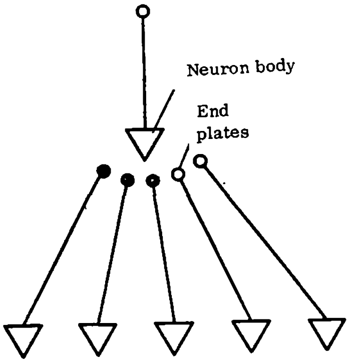

Figure 82. Symbolic Diagram of Nerve Network.

W. McCulloch and W. Pitts [5] were the first to simulate nerve networks by means of model neurons. In addition to the indicated conditions, they also introduced the following: the transfer of stimulation from one neuron to another occurs with a delay per unit time and the entire nerve network operates in a single rhythm. Under these conditions, which clearly simplify the existing physiological laws, the trial-and-error method can be used to find the network structures which simulate actual logic actions, e.g., counting to four followed by a signal indicating the termination of the count. Electronic simulation methods make it possible to find variations of nerve networks composed of model neurons which possess extremely diverse properties. According to the probability theory, the greater the number of neurons in a nerve network, the more authentic the simulation of nerve activity of an actual brain.

The work done by B. Farily and W. Clark is of much interest. They employed a digital computer for simulating the activity of a complex self-organized system on the basis of the principles of the nerve network [6]. It turned out that the entire system was capable of self-organization under certain logic conditions and with the selection of appropriate neuron-stimulation thresholds, i.e., the system can quickly return itself to its initial state when it is withdrawn from the state of stable equilibrium.

Taylor has developed models of neurons and synaptic contacts on the basis /270 of capacitors and resistors which are stimulated by 1-msec square pulses. He constructed a nerve network from these elements which performs a number of given operations, e.g., the separation of maximum amplitudes or given frequencies [3].

Nerve networks are being developed at the present time with plastic neurons which change their thresholds in accordance with the given conditions. Neurons also have been proposed with several inputs which possess a greater information capacity and assume a greater number of various probability states, respectively [7].

A complex neuron structure possesses high reliability due to the expressed redundancy of its organization, while individual neurons have extremely low reliability. Living organisms are highly reliable cybernetic systems which are constructed from unreliable elements. The increase of reliability is truly the most significant problem of modern engineering. A contemporary aircraft contains up to 100,000 electronic components which are connected into a complex system. Bionics provides the key to high reliability of similar systems. The opinion exists that one of the fundamental tasks of bionics is to study the possibility of increasing reliability by means of the appropriate use of unreliable elements.

The problem of developing highly reliable engineering systems from unreliable elements was first studied by the famous mathematician, John von Neumann [8]. He indicated that the efficiency of a system could be improved by combining unreliable elements in a specific manner. He proposed that the tremendous redundancy of elements is the basis of the reliability of biological systems. Redundancy makes it possible to quickly replace components that have gone out of order, while the parallel operation of a large number of components makes the malfunctioning of one or several components unessential in the majority of cases. The principle of redundancy is now being used quite frequently in engineering to increase reliability. There is "cold" and "hot" redundancy. "Cold" redundancy denotes that the system has components which are ready to replace the malfunctioning components but are in a non-operating state. Several identical components which operate in parallel are utilized in "hot" redundancy.

Modern engineering has given birth to a special science, i.e., reliability theory. The task of this science is to investigate the causes of malfunctioning of complex devices and to seek methods of increasing their service life. Reliability is the ability of any technical device to perform all of its intended- /271 functions, i.e., to operate unfailingly and to preserve its original technical specifications during a given time and under corresponding operating conditions [9, 10]. The rapid rates of scientific and technical progress have raised the problem of increasing quality, i.e., the problem of reliability, to first place. The study of the reliability of engineering systems has indicated a characteristic law which states that the maximum number of failures is observed in the first period after the manufacture of a system. The assured life of an item is established in accordance with the rated value of the time of the maximum number of failures. A long period of normal and trouble-free operation is then observed, when malfunctions are rare and theoretically not very probable. Finally, as a result of the natural wear of parts and aging of the machine, the number of failures sharply increases. An analogous situation is observed in the development and activity of a living organism. The maximum number of diseases is noted in childhood, since the organism has not yet matured and has not been exposed to the influence of various factors. If the organism has matured and become resistant, it will generally not become diseased during the course of its entire subsequent life. The number of "failures" then increases in old age. It is the result of natural aging. This analogy between the reliability of a living organism and complex engineering systems provides us with a basis to think that the discovery of the "secrets" of ensuring reliability in an organism will make it possible to work out effective measures for increasing the reliability of engineering systems.

The study of the nervous system has indicated that extensive redundancy of elements is one of the most important principles of its reliable functioning. This principle is being actively used in engineering at the present time. It is, however, only one of many principles. We should not forget the fundamental distinction between the elements of biological and engineering systems. We are bearing in mind the metabolism in the organism. The continuous revitalization of the structures of a living organism due to the constant processes of destruction and restoration is an extremely important factor of stability and reliability. The idea of creating self-regenerating engineering systems is being studied at the present time, but it is still quite far from practical realization. On the basis of an analysis of currently known physiological data, E. A. Asratyan and P. V. Simonov made a number of interesting statements concerning the reliability mechanisms of the brain [11]. The process of protective inhibition has an important value for providing the brain with high reliability. The transition of nerve cells to an inhibitory state in this case can be considered /272 as the active intervention of the organism in the activity of its elements and their transition to a nonoperating state in order to restore decreased efficiency, i.e., "preventive maintenance". Another important reserve of reliability are universal components which can replace any components that have gone out of order. These components are capable of rapid functional rearrangement and learning (flexible programming of spare parts). Finally, another mechanism of reliability which is important to engineering is the expediency of combining self-control with central regulation. The liberation of the higher regulatory mechanisms from the responsibility of looking after the lower mechanisms makes them more reliable, while the subordinate systems can function independently for a certain length of time in the event of the failure of the "command" centers.

The high reliability of biological systems is stipulated by the good "mutual awareness" of elements. A control process, as we know, is above all an information process. The reliability of control depends upon the reliability of the collection, storage, and transmission of information. A living organism is distinguished by a high degree of intercorrelation between functional and morphological characteristics, and it reacts as a single entity to each "disturbance", whether it is local or not. A tremendous amount of research has been devoted to the problem of the participation of the nervous system in the various reactions of the organism to the influence of environmental factors and in the organization of a pathological process. All of this research is actually related to the study of the reliability mechanisms of the organism and the role of the nervous system in providing reliability. Cybernetics compels biologists and physiologists to pay particular attention to the informational aspect of the phenomena which they are studying. Bionics is interested in transferring the elements of the highly reliable informational structure of living organisms to engineering. The time has now arrived when even extremely specialized biological investigations are of interest to other sciences, including such disciplines remotely related to biology as engineering.

Research on Analysor Systems and the Problem of Image Recognition

The analysor systems of living organisms are highly organized formations which have no equals in contemporary engineering equipment. The eye is sensitive to a single light quantum. The heat sensor of the rattlesnake distinguishes 0.001° temperature variations. The electrical organs of fishes sense potentials of a fraction of a microvolt. Transducers with these characteristics could essentially affect the course of technical progress in scientific research. Analysors are 3-component systems which consist of a receptor, conduction path, and a brain center. Each of these components has operating principles which are extremely interesting to engineers. The study of these principles has only just begun. Let us consider the most important analysor, i.e., the visual organ, through which there proceeds over 90% of all the information to the human brain. Each eye has 10^8 photoreceptors which are connected to the brain by means of 10^6 ganglionic cells (100-fold redundancy of photoreceptors). Several features of the visual analysor which are interesting from the engineering point of view should be noted. /273

1. The sensitivity range of the retina is from a few light quanta to the luminous fluxes which occur when looking at the sun.

2. Visual clarity varies from the center to the periphery.

3. The eye adapts to static images. The eye accomplishes small oscillatory motions at a frequency from 1 to 150 Hz when looking at stationary objects.

4. The eye continuously and automatically follows moving objects.

A thorough investigation of these characteristics of the eye could provide a key to the solution of a number of important engineering problems and automatic systems could be developed on this basis to control the amount of light which strikes a light-sensitive instrument, which would provide uniform sensitivity in a wide range. The development of methods of effectively encoding data on speed and measuring the position of a scanning beam in devices which pick up images is also of interest. An automatic spatial-depth finder is currently being developed (e.g., for analyzing aerial photographs) on the basis of the recently discovered possibility of spatial-depth [three-dimensional] perception during monocular vision.

The work being done on an artificial retina which will be analogous to the retina of a frog is of interest. The work accomplished by J. Lettvin and his associates [12] at the Massachusetts Institute of Technology has resulted in the discovery of many properties of the visual apparatus of the frog, particularly the significant role played by the ganglionic cells when performing complex operations during the transmission of images. A frog's eye contains five types of ganglionic cells which are distinguished by the shape and size of the /274 dendrite branchings. Each of these cells performs a particular function: e.g., determines the boundaries of an image, the movements and contrast of an object, etc. The visual centers of the brain have corresponding layers of nerve cells which perform the same function (image interpretation). The artificial retina consists of three layers of neurons: receptors, bipolars, and ganglionic cells. The first layer includes 1800 photoreceptor cells. The bipolars are neurons which pick up positive and inhibitory signals from the photoreceptors and determine the image contrast. The third layer contains 650 ganglionic cells of five types.

A frog's eye can distinguish circular shapes. This function was simulated by Harmon by means of seven photoreceptors and one artificial neuron [16]. The neuron is stimulated when the central photoreceptor is completely shaded or when a certain threshold of the weighted sum of the signals of the six other receptors is reached. The initial adjustment of the device provides for mutual compensation of the output signals of inhibition and stimulation when all receptors are uniformly illuminated.

Work is being conducted on the simulation of the human and animal auditory analysor. The exceptional sensitivity of this analysor is indicated by the fact that individuals with acute hearing perceive sounds at the magnitude of sound pressure in the auditory meatus of approximately 0.0001 dyn/cm^2, which corresponds to a movement of the cochlea of 10^{-11} cm (approximately 1/1000 the diameter of a hydrogen atom). The idea of achieving similar sensitivity in engineering devices is very alluring. Scientists are also attracted to the problem of information transmission from the ear to the auditory region of the brain. It has been demonstrated that the ear functions as a band filter, which converts signals with a time distribution into signals with a space distribution.

The RCA firm is developing a system for processing verbal information [16]. Many well-known psychoacoustical phenomena are considered in this system. The action of the cochlea is simulated by low-frequency RLC circuits. The output signals enter the first network. The first layer of electronic neurons emphasizes the small distinctions in amplitudes of the signals of adjacent channels, the second layer selects the optimum signal from two adjacent neurons, and the subsequent layers extract the local maxima and minima and local plus-minutes of the transitions.

Going on to the olfactory organ, the existence of engineering analogs of this analysor should be pointed out. The olfactory organ in certain animals /275 plays a significantly more vital role than the human olfactory organ. Dogs possess an extremely high capability of distinguishing odors. Certain fishes sense various odoriferous substances in concentrations of a few milligrams per liter. Experiments have been described where rats were taught how to recognize schizophrenics by their odor. The first attempt to create an artificial olfactory device (electronic nose) was made by the American scientist, Dravnicks. He designed a device which distinguishes three odors: acetone, thiophene, and pyridine. More sophisticated devices are currently being developed [17].

Many living organisms have analysor systems which man does not possess.

Heat sensors are found in birds, insects, fishes, and reptiles. Crickets have a smooth tubercle on the thirteenth segment of their antennae which picks up infrared radiation. Sharks and rays have so-called Lorenzini ampulla (channels on the head and in the anterior portion of the body) which enable these fishes to detect 0.1° variations in water temperature. Certain birds [translator's note: Russian term for this bird is "Meli"; might possibly be a "Malay" bird in English] maintain a constant temperature in their underground nests with an accuracy to 5° while the outside temperature may fluctuate up to 30°. These birds regulate the heat by raking the sand that covers the rotting leaves which line the bottom of the hole.

Snails and ants [18], and also rats [19], are sensitive to radioactive emission.

Electro-sensitive organs have been detected in fish. It has been proposed that the behavior of a fish before a storm (it makes a deep dive) is explained by the reaction to stray currents in the water basin which are caused by electrification of the air. A report was recently published concerning the formation of dense swarms of mosquitos which flew in definite isolated routes within the limits of an artifically created electrical field. It has been proposed to use this phenomenon to combat harmful insects. Certain animals sense subsonic and ultrasonic oscillations very well. Ultrasonic ranging and detection in fish and bats has been quite well studied. Dolphins emit vibrations in the 150-155 kHz range. Devices for studying these signals have been developed [20]. Certain fresh-water fishes accomplish sonar at frequencies below 16 Hz. Jellyfish react to the subsonic vibrations that occur before a storm. Bats emit ultrasonic vibrations in the 30-110 kHz range. It is interesting to note that the moths which are eaten by bats have organs that are sensitive to the indicated vibration spectrum. Owls also have "ultrasonic receivers" to detect bats. /276 The arrangement of miniature and reliable sensors, i.e., the organs of living organisms which possess high sensitivity to various signals of the outside world, is of tremendous interest to engineers. A knowledge of the principles of action of these organs would make it possible to advance many fruitful technical ideas. Proposals have recently been made concerning the creation of engineering systems with biological sensors: e.g., using bees' eyes to detect ultraviolet rays and cockroach eyes to detect infrared rays.

Perceptrons. In examining technical models of analysors, we should mention the so-called perceptrons. They are self-organizing "learning" systems which perform the logic functions of recognition and classification. Perceptrons correspond to brain centers, in which information is processed and perceptions are formed. An enormous amount of research has been devoted to the recognition of visual images and there have been some studies on the recognition of other signals, e.g., speech.

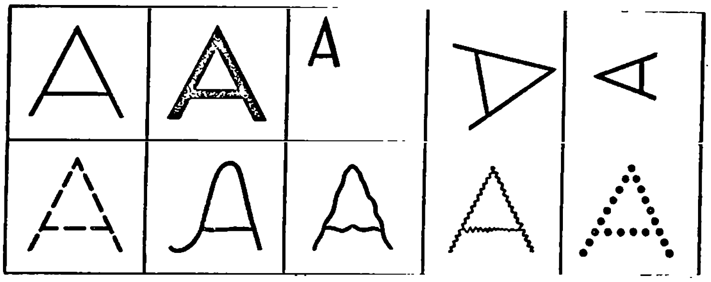

Figure 83. Examples of Isomorphic Transformations of the Letter "A".

The recognition of any object is the formation of a certain signal or code which has a one-to-one correspondence to the object being identified. Recognition should be accomplished independently of the isomorphic transformations of the object, i.e., those transformations, as a result of which the scale, brightness, and orientation of the image can be changed, but its basic value is retained. Figure 83 illustrates an example of isomorphic transformations of the representation of the letter "A". One of the first self-organizing recognition systems was the MARK-I computer. It recognized any letter of the alphabet in 100% of the cases after it had been shown the letter 15 times with a "confirmation" of the correct answer [18]. The human operator trains /277
the perceptron: he shows it images, points out errors, and confirms correct reactions. The perceptron is based on the theory of statistical discrimination and requires preliminary programming for its operation [21].

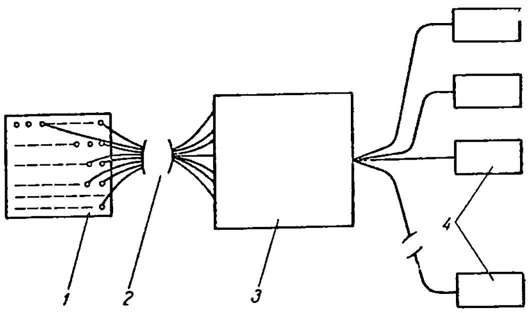

Figure 84. Block Diagram of Perceptron. 1 = Receptor Field; 2 = Random-Association Block; 3 = Association-Cell Block; 4 = Effector Cells.

The block diagram of a perceptron is shown in Figure 84. The input unit is a receptor field. When visual images are to be identified, the receptor field is a set of photocells. The association-cell block is randomly connected to the receptors. If the sum of positive and negative signals sent to an association cell from the receptor field is positive and exceeds a certain positive value, this cell sends a signal to an effector cell. The total value of the signals sent to the effector cell is automatically compared with the given threshold value, as a result of which an output signal is generated. By varying the parameters of the association cells (they are neuron analogs) the operator gets the correct reaction from the perceptron. After a certain period of "instruction", the perceptron can make "independent decisions".

The MARK-I has 20 times more memory components and a more complex system of interrelationships than other computers, which considerably expands the machine's capabilities.

The problem of developing automatic recognition systems is of much practical interest. Serious research is being conducted in this area. A recent report indicates that the General Electric Company is quite interested in the visual organs of the king crab (Limulus). The eye of a king crab can intensify the contrast between the edges of a visable image and the background. Attempts are presently being made to create an electronic device which would simulate the /278 action of the king crab's eye. This device would be used in a television camera to magnify the contrast of x-ray negatives and aerial photographs [22].

The creation of automatic devices for recognizing visual images is based on extremely detailed physiological investigations of the visual analysor. The monograph by B. D. Glaser and I. I. Zukerman, Information and Vision [23], is a significant contribution to this problem. The authors propose that a biological system for recognizing visual images is based on unconditioned-reflex and conditioned-reflex mechanisms. Unconditioned-reflex mechanisms are used to detect simple configurations. Recognition of complex images is based on the analysis of profound statistical relationships in the image and must be learned. Thorough electrophysiological investigations are making it possible to derive a detailed concept of the work of the individual elements that make up a biological recognition system. Definite progress has already been made in this direction. N. D. Newberg established some of the mechanisms for encoding color information in the retina [24]. A. L. Byzov studied the signal-processing mechanisms in the retina [25]. M. M. Bongard successfully simulated the process of learning how to recognize images with the aid of a general-purpose computer [26]. A. G. Arkad'yev and E. M. Braverman experimented with teaching machines how to recognize images; the process of recognition learning was programmed in the course of these experiments, regardless of the type of visual image which the machine had to recognize [27]. V. P. Sochivko's works are devoted to the general theory of automatic recognition [28].

A great deal of importance has recently been ascribed to problems of recognizing various types of information. The theory of automatic image recognition has been formulated and is developing rapidly [26, 27]. Since the practical result of the recognition theory is the construction of various automatic information and logic systems, an examination of this theory in a section dealing with bionics is fully justified.

Recognition devices simulate the work of sense organs: visual, auditory, and tactile. The object of recognition may not only be images, but also sounds, e.g., an operator's voice or complex motor acts. Let us examine the recognition process in more detail. The receptor of a recognition device provides image information in a form which is suitable for input to the subsequent units. The term "image" can refer not only to visual objects. An image in the form of electrical signals is filtered and noise is removed from it. In some cases preliminary /279 recognition is accomplished in the filter. For example, there are so-called sampling filters in which there occurs preliminary recognition of the elements which make up the image and selection of these elements according to definite characteristics. It was assumed until recently that the perception of visual sensations is the result of the transmission of a mosaic system of impulses to the brain. These impulses were thought to be duplicates of the spatial distribution of light stimulations on the individual elements of the retina. Current research indicates that the function of the retina is more complex and that the eye sends a preselected, highly organized signal to the brain. The eye, thus, functions as a sampling filter and as a device which preliminarily processes information selected from input signals in accordance with the internal structure of the device.

Recognition is naturally accomplished in an association system. A signal which enters this system is a description of the object or its image. The object's image is compared with standard images and matchings are determined. The object's image is referred to a definite class of images as a result of recognition. The class of images to be identified is a combination of elements and standard images which are incorporated into one set. We previously mentioned that the isomorphic transformations of a recognition object are factors which hinder the operation of recognition devices. Isomorphic transformations should not withdraw the original from the field of action of the recognition device which characterizes the system's capabilities.

The theory of automatic recognition utilizes extensive mathematical apparatus. Set theory and mathematical logic are especially important. The solution of recognition problems requires the development of special algorithms. These algorithms are ideally mathematical representations of the elements of psychophysiological analysor activity.

Most of the research to the present time has been devoted to so-called quasi-visual recognition, i.e., the creation of devices which simulate vision. Recent investigations have been conducted in the area of quasi-auditory and quasi-tactile recognition. The importance of the work being conducted on quasi-auditory recognition requires no explanation since the chief means of communication between humans is speech. The recognition of voice commands for control purposes has been the object of numerous investigations for some time [16, 29]. Automatic speech recognition will make it possible to control machines without preliminarily instructing man how to manipulate a very complicated set of handles /280, buttons, and pedals. N. P. Sapozhkov's special monograph [30] presents a detailed examination of the problem of employing devices to recognize speech in communication systems and various cybernetic devices. There are other aspects of the problem of quasi-auditory recognition. The work being done on the automatic recognition of sounds made by malfunctioning machinery is of practical importance: e.g., the sounds made by malfunctioning aircraft engines. Automatic recognition of the sounds made by the sea will make it possible to predict swells and gales [1]. One of the solutions to the problem of early detection of gales based on simulating the reactions of the jellyfish can be cited as an example. It was discovered that this extremely simple sea creature "hears" subsonic vibrations which cannot be picked up by human hearing. These vibrations propagate well in water and occur 10-15 hours before a gale [31]. The M. V. Lomonsov Moscow Institute has developed an instrument which consists of a horn, resonator, piezoelectric amplifier, and meter (Figure 85). The importance of this project is evident from the fact that many special stations, sonar and radar installations, and meteorological facilities are presently being utilized for early detection of storms, and plans have also been made to employ special artificial earth satellites, i.e., weather observers. The methods of quasi-auditory recognition have an important military significance for the early detection of enemy ships and submarines. /281 Automatic self-organizing quasi-auditory devices known as "Cyberons" are being developed for these purposes [1]. These "Cyberons" are being designed by an American firm, the Raytheon Company. The C-100 system, according to the American press, can quite effectively recognize the noises made by submarines. The C-200 "Cyberon" is being designed to recognize all phonemes of the English language.

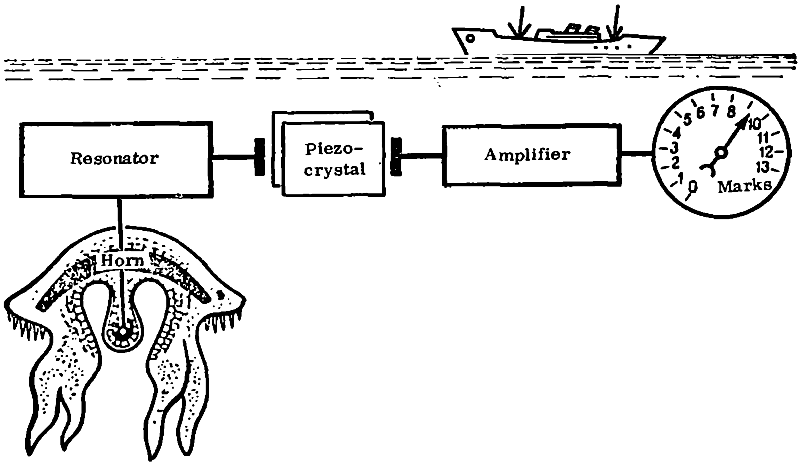

Figure 85. Device which Simulates the "Auditory" Organ of a Jellyfish.

Quasi-tactile recognition is a simulation of the tactile organs. Mechanical contact of a receptor device with the object to be identified will make it possible to recognize shape, volume, and terrain features.

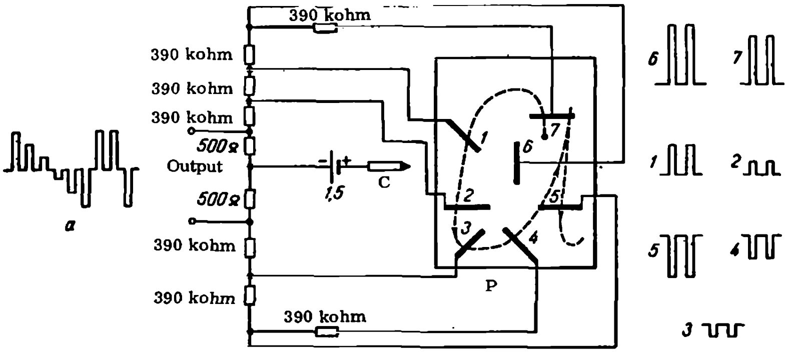

Figure 86. Device for Converting the Motor Acts of Writing (Handwriting) into Discrete Electrical Signals. P = Platform with Built-in Conductors (Probes); C = Contact Pencil; Samples of Signals from Individual Probes are shown on the Right (Designated by Numbers); A Sample Tracing Obtained by Writing the Letter "a" is Shown on the Left.

An example of the ever increasing application of the theory of automatic recognition in various fields of science is the research being conducted on the recognition of written signals [22]. Printed texts have been recognition objects until recently. Work on the recognition of handwritten texts is going very slowly. However, entirely new possibilities will be opened if we study not the result of writing in the form of a manuscript, but the process itself, i.e., the motor act of writing. R. M. Bayevskiy has proposed two types of instruments for converting the motor acts of writing (handwriting) into electrical signals. One of these devices generates handwriting signals in analog form and the other generates signals in digital form. The first device is a mobile platform with one or two degrees of freedom. The platform moves together with a pencil which /283 writes characters on a piece of paper attached to the platform [41]. The platform's movements are converted into electrical voltage by an electromagnetic pickup. The second device is a stationary platform with conductors built into it. The conductors form a system of probes as described by the theory of quasi-visual recognition (Figure 86). The pencil traces a written character and alternately closes the probes. Electrical signals of retangular shape then appear at the output of the device. Each written character, or, to be more exact, each motor act, is characterized by a definite sequence of signals, duration of intervals between them, and length of the signals themselves (Figure 87). There are two trends in the development of this new field: the diagnostic and the bionic. The diagnostic trend is to work out methods of investigating the functional state of the motor analysor and to coordinate movements by means of analyzing handwriting signals. The bionic trend is associated with the creation of

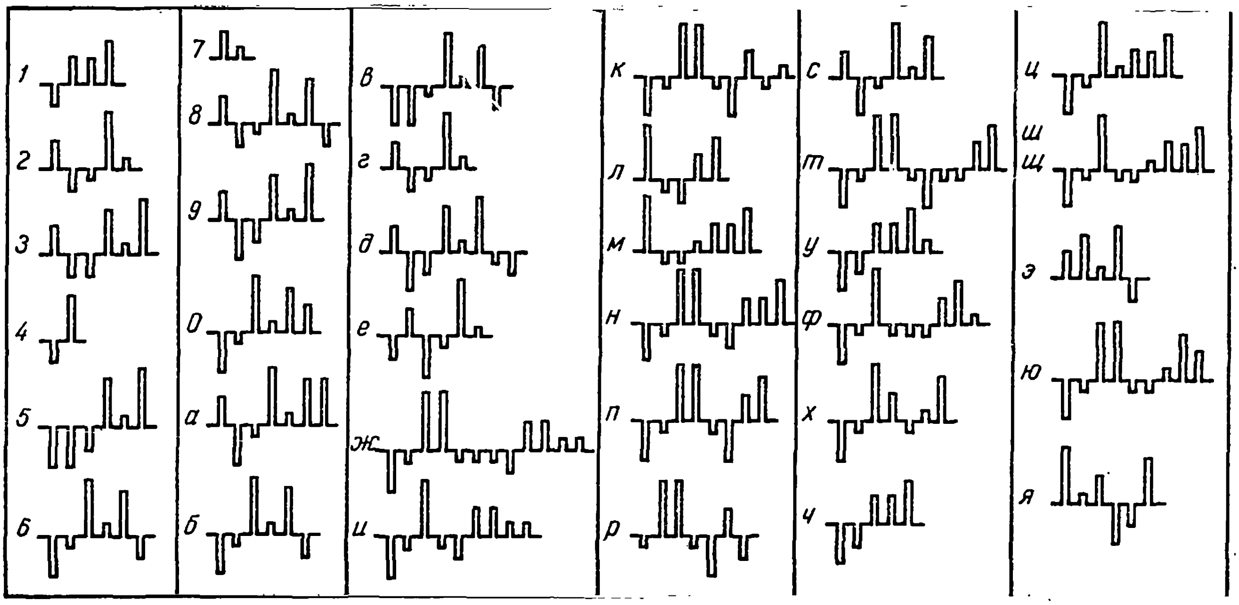

Figure 87. Discrete Code of Numbers and Letters. Tracing Obtained with the Device Illustrated in Figure 86.

automatic control systems which would be governed by the motor act of writing. It is quite probable that symbols which are easily remembered and reproduced by an operator may contain extremely complex sets of instructions whose memorization and reproduction would require extensive study. Questions of optimal encoding of written signals may also be employed in the development of effective communication systems.

Studies are presently being conducted on the analysor systems of biological objects from the standpoint of their receptors, as well as with respect to the central formations which carry out signal recognition and synthesis. The engineering application of the knowledge derived from these studies will soon make it possible to create a large number of new technical devices which will essentially expand the possibilities of "discourse" between man and machines. Figure 88 illustrates the current status of the "man-machine" problem in the sense of its technical capabilities. As can be seen, man presently has only one real channel for feeding into a machine (motor commands: buttons, pedals, printers). Information can be sent from a machine to man over the visual and auditory channels. The number of these and other channels may soon be essentially expanded. The appearance of at least 7 new channels may be assumed for feeding information to a machine: speech channels, writing channels, physiological-/284 information channels, and channels for the input of information on the spatial position of man (television, cyclography, etc.). Proprioceptive, tactile, and olfactory channels may be used to feed information from a machine into the human central nervous system. The further development of bionics will make it possible to more uniformly load the analysor systems of man, which will thereby increase the effectiveness of control and the reliability of man as the components of complex systems.

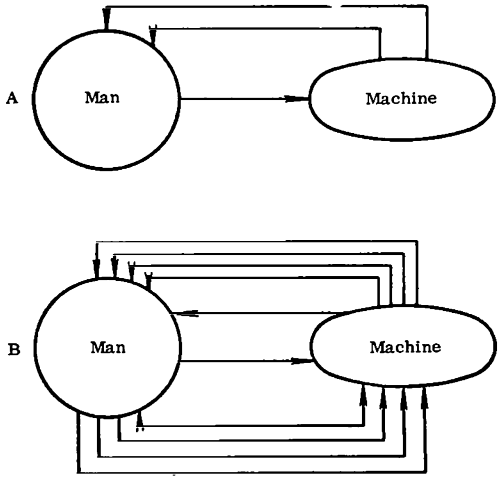

Figure 88. Communication Channels in a "Man-Machine" System Today (A) and Tomorrow (B).

Detection, Orientation, and Navigation in Living Organisms

The rapid development of electronics and computer technology has led to the creation of powerful engineering systems for detection, orientation, and navigation. These systems have been used a great deal by the army, navy (submarines), and the air force (spacecraft). The necessity of solving such problems as the detection of enemy aircraft and missles, the determination of a submarine's position on a long cruise, and orientation in space flight have led to the fact that extremely complex radioelectronic equipment has become an inalienable part of aircraft, submarines, and spacecraft. Special ground /285 stations for guidance, detection, and tracking are bulky and costly structures. At the same time, biologists know of many living organisms which possess systems of detection, orientation, and navigation that are considerably more sophisticated than those existing in engineering.

Sea turtles float in the sea for several thousand kilometers, but always return to the same place on the shore to lay their eggs. It has been proposed that they have a system of distant orientation based on stars and a system of near orientation based on odor (the chemistry of the water near the shore).

The detection system of butterflies is very interesting. Bees and wasps orient themselves very well on the sun. The independent elements of their globular eyes (omatidia) admit light of different intensity depending upon its direction. Light polarization makes the brightness of the sky unequal in each optimidium of the bee. Orientation is not disturbed even when the sun is covered by clouds.

The navigational capabilities of pigeons are well known. There is an hypothesis concerning the pigeon's sensitivity to the intensity of the earth's magnetic field.

Experiments were recently conducted to explain the orientation mechanisms of robins which migrate from Europe to Africa and back. The experiments were conducted in a planetarium during different seasons. It was discovered that robins distinguish individual patterns in the stellar sky and know how the position of stars in the sky changes at night and how the picture of the stellar sky changes in the different seasons. The experiments also indicated that a robin's ability to orient itself on the stars is inherent. An understanding of the robin's ultraminiature and absolutely reliable system of remote stellar navigation would be of obvious use to science and engineering [31].

Simple electricity-based systems of short-range detection also are of definite interest to engineers. A 30-200 microvolt electrical field is formed around the heads of lampreys at a distance of several centimeters. Small animals that fall into this field change the voltage distribution, which serves as a unique signal to the lamprey. African fresh-water tropical fishes (Mormirus) search for food by emitting an alternating field (100 vibrations per minute). The emitter is located in the tail. The receiver is on the back. The range of this detection system is several meters.

A great deal is also learned from such generally known facts as how certain plants (sunflowers) follow the sun's position in the sky, the remarkable ability /286 of cats to return "home" even from extremely far places, and the migration of fish. The investigation of these questions was once the exclusive prerogative of biologists, but has now entered the realm of bionics and is of exceptional importance for further technical progress.

The importance of studying a number of biological systems for the purpose of utilizing the subsequent knowledge in engineering is illustrated by a table (see Table 17) of comparative data on a modern radar and the echo range and detection apparatus of a bat [32]. As we know, bats make up a highly specialized group of mammals which are distinguished by active flight and have acquired a special method of maintaining contact with their environment in the course of their evolution. This method is based on the animal's transmission of discrete ultrasonic impulses with the subsequent reception of echos reflected from surrounding objects. Various types of bats have different parameters of emitted signals and various echo-reception methods.

TABLE 17. COMPARISON OF THE EFFECTIVENESS OF ARTIFICIAL AND NATURAL RANGING AND DETECTION.

	Radar	Sound-detection apparatus of bat	
		large	small
object to be detected	aircraft	insect	wire
size of object, cm, d	300	1.0	0.02
range of detection, cm, R	$8 \cdot 10^6$	200	90
weight of apparatus, g, W	$9 \cdot 10^4$	1.0	0.5
power output, w, P	10^4	10^{-5}	10^{-6}
P/RdW	$3 \cdot 10^{-5}$	$2 \cdot 10^7$	10^{10}

The research conducted by A. I. Konstantinov at the E. Sh. Ayrapetyanets Laboratory on the physiology of the spatial [three-dimensional] analysis inherent to bats is of much interest [33]. He established that the basis of spatial analysis is the generation and subsequent performance of conditioned reflexes. He has expressed the opinion that there are forms of information which are still unknown to science. These forms of information, which are important for further technical progress, act upon the analysor systems of bats and help them to find their shelters at distances up to 20 kilometers (homing) without visual reception.

Research on the Morphological Characteristics of Living Organisms as a Task of Bionics /287

Bionics is presently investigating not only the information systems of living organisms, but also their morphological characteristics. It has been discovered that the skin structure of fast-moving aquatic animals provides the key to increasing the speed of a ship. A dolphin's skin possesses the property of nonwettability (hydrophoby) and has an elastic shock-absorbing structure. This eliminates turbulent vortices and permits the dolphin to glide through the water with minimum resistance. A special artificial skin has been developed, called "laminflo", which consists of three layers. The upper layer is smooth, the middle layer is elastic and has flexible rods and a damping fluid which fills the cavities between them, and the lower layer is a sheathing. A torpedo model which was covered with "laminflo" skin developed a speed 50% higher than a control model without the skin. The use of thick cushions in the bow of a vessel (by analogy with the thick fatty areas on the head of a dolphin) may make it possible to retain the speed of vessels in the event of a large wave [34].

The principle of the gyrotron was borrowed from the insects. This device provides a high degree of stabilization of the selected direction of flight of an aircraft at high speeds. Dipterons have balancer appendages which continuously vibrate together with the wings. When the direction of flight is changed, the direction of motion of the balancers does not change, and this stretches the petioles which connect the balancers to the body. The insect receives a signal on the change in flight direction. The gyrotron is a forked vibrator which is controlled by an electromagnet. An aircraft with a gyrotron can be automatically pulled out of a spin [35].

Insect flight is extremely effective with respect to energy consumption. It has been calculated that a bee utilizes approximately 9% of its payload in its movements. One of the reasons for the highly effective "engines" of insects is the peculiar motion of their wings, which have a figure-eight shape. Wind turbines with moving vanes that have been developed on the basis of this principle have turned out to be extremely economical and can operate even in an extremely low-velocity wind. Thus, engineering solutions based on living prototypes may be an essential contribution to modern technical progress. It should also be noted that many engineering solutions which were found with difficulty in the "pre-bionic" period have been known in nature for some time. For example, /288
aircraft anti-flutter equipment (thickening of wing edges), which provides structural stability during vibrations, has an analogy in the insect world. Bifocal lenses for correcting vision defects are analogous to the eyes of certain fish in which the upper portion of the eye is for distant vision and the lower portion is for near vision. The periscope has also existed for a long time in nature: e.g., the periophthalmus fish.

A significant number of problems has recently appeared in which the joint research of biologists and engineers could be extremely fruitful. We shall mention only a few of those connected with the morphology of living organisms:

-- the flight of insects and birds as the basis for the creation of new flight vehicles;

-- the muscles as the most economical engines;

-- the design of joints as the principle of construction of "eternal" bearings;

-- the motion of leaping animals, the kangaroo in particular, as the basis for developing all-purpose, wheel-less vehicles.

The Future Development of Bionics

Bionics is still in its infancy, but its main task, i.e., seeking living prototypes for the creation of new technology, well defines its future development for many years to come. Bionics takes in many areas and is related to many disciplines. There could hardly be specialists in bionics in the broad sense of the word. By smoothing out the contradictions between biology and the engineering sciences, bionics is creating a common language for scientists of different specialities, e.g., for physicians and engineers.

Since it is an engineering discipline in science to a significant extent, bionics will undoubtedly be of use to biologists as well. Bionics requires the construction of effective and practically useful models based on data obtained from biological research.

This makes it possible to approach the practical verification of theoretical concepts in biology, which is a progressive step in explaining the laws reflected in the objective world. Bionics requires the synthesis of phenomena, while analysis and verbal description predominate in biology. In addition, a working contact with engineers will promote a significant increase in the technical, mathematical, and physical education of biologists and will also lead to /289 the introduction of modern exact research methods in biology.

In addition to the trends of bionics which were described above, other areas obviously will be developed. For example, the "biological clock" is of much interest. Animal organisms are able to note a change in the season, the time of day, and even shorter time intervals.

Nature has extremely sophisticated technological proceses at its disposal with regard to the synthesis of a tremendous amount of matter. A study of the "technology" employed by nature will make it possible to significantly accelerate the development of chemical synthesis.

The study of phosphorescent sea creatures and the electrical organs of certain fishes may provide a key to the development of new methods of obtaining luminous energy and electrical power.

The study of natural processes has already led to the creation of a new principle for obtaining electrical power. We are speaking of the biochemical fuel cells. The structure of one of these cells is shown in Figure 89. The fuel cell consists of two sections divided by a semipermeable partition. There are inert cathodes inside the sections. The anode section contains the "fuel", i.e., a mixture of sea water and organic matter, and also a catalyst, i.e., bacterial cells. The cathode section contains sea water and oxygen. The operation of the fuel cell is analogous to processes of oxidation and decomposition of organic matter near the bottom of the ocean, which leads to the generation of electrical energy [1].

The direct conversion of chemical energy into mechanical energy is of much interest. As we know, this process is accomplished during muscular activity. A model of a muscle based on giant molecules of polyacrylic acid has recently been developed [36]. A film strip is made from this acid. Upon entering an acid medium, the strip enters a state of disorderly twisted chains. When the medium is changed to an alkaline one, the molecules are charged by negative charges which repel one another, and the film strip is straightened. If the film strip is attached to a weight, a change in the medium can cause it to accomplish work, e.g., to lift the weight.

We shall take our last example from the field of genetics. As we know, nucleic acids store hereditary information. They are unique punched cards of a biological system. We also know that the methods of encoding information in DNA molecules are extremely economical and their code is exceptionally interference-free. The study of this problem will undoubtedly be of interest to engineers working in the area of information storage and retrieval systems.

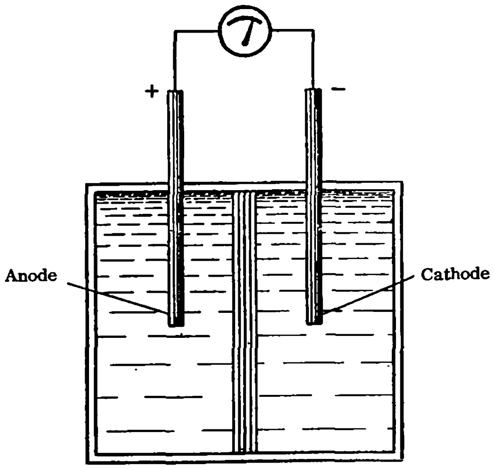

Figure 89. Fuel Cell.

We mentioned above that bionics is /290 smoothing out the contradictions between the biological and engineering sciences and is transforming biology from a user of technology into a source of new technical knowledge, i.e., into a means of technical progress. This in turn arouses a great deal of interest in engineers with regard to the results of biological research. However, this also imposes serious obligations on biology. The work done in the field of bionics can be based on a knowledge of the laws of the structure and functioning of biological systems. This knowledge is clearly insufficient today since it is essentially qualitative, while technical utilization requires that it be expressed in the form of mathematical descriptions, tables, and graphs. Therefore, the majority of publications, even those which contain data which is of interest to engineers, cannot be utilized by bionics and must be employed at the appropriate level. The revolutionary role which bionics plays in biology is that it is re-educating biologists with regard to contemporary mathematical, physical, and other exact methods. Thus, bionics is assisting in the development of a language which is common to biology and engineering, i.e., a language which can be understood by representatives of both fields, and which thereby brings them closer together.

Bionics is an extremely promising scientific discipline. We will undoubtedly witness the extensive development of various aspects of bionics in the very near future. The joint work of biological specialists and engineers will make it possible not only to quantitatively interpret the already known biological laws, but will also result in the discovery of qualitatively new principles /291 of organization and functioning of biological systems. In addition to the research trends which were considered above in sufficient detail and are being further developed, it is possible that the following problems may become subjects of joint biological and engineering research:

-- the problem of simulating biological systems or their components by technical means; the creation of bioanalogs as separate engineering devices or in the form of components of complex engineering systems;

-- the problem of utilizing living systems as input or output devices in complex engineering systems.

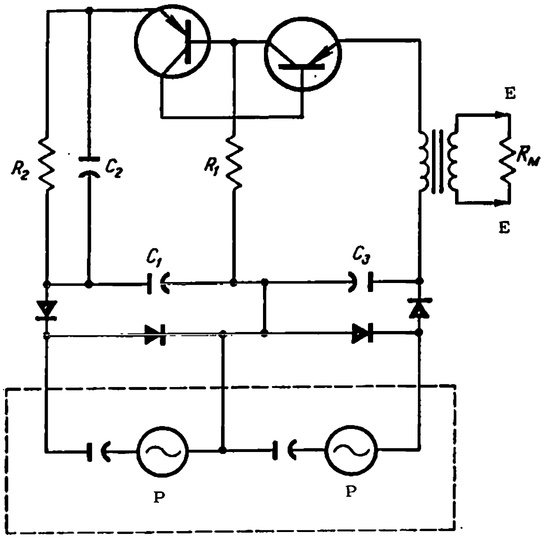

Figure 90. Circuit Diagram of a Device for Autostimulation of the Heart. Piezoelements (P) Sutured to Aorta Wall. Energy Produced by Generator is Fed to the Electrode (E) in Region of Pacemaker.

There is already some information on the use of insects as components in the following systems [37]:

-- the problem of organizing very large systems; analysis of the construction and functioning of multicellular structures, neuron networks, and multicomponent systems of biological origin;

-- the problems of control and information /292 processing in biological systems. An important value is ascribed here to the stability of biological systems toward external influences and to control methods which would provide this stability. Questions of information encoding, transmission, and storage in biological systems at various levels (cell, organism, group of organisms);

-- problems of bioenergetics and biomechanics. Investigation of complex biological and biophysical processes at different levels. The problem of utilizing the energy of living organisms for obtaining external energy is considered here. The first investigations in this area have indicated, for example, that the motive energy of an animal can be converted by means of a special transducer into electrical energy to supply the power for a tunnel-diode telemetry transmitter (Figure 90). Works have also been published recently concerning the utilization of energy derived from cardiac activity and muscle contractions [38, 39], and also the direct use of the biopotentials of a living organism [40].

The trends in the development of bionics can be summarized in a more general form with regard to the levels of organization of biological systems:

-- molecular and submolecular bionics

-- bionics of cellular structures

-- bionic research on functional systems and organs

-- bionics of entire organisms

-- bionic aspects of the interrelationship between living organisms

-- bionic aspects of the "man-machine" system.

In conclusion, it should be noted that the tremendous prospects for the development of technology in association with the study of natural experience acquired in the organization of biological systems do not signify that all the known or recently discovered biological laws can be practically utilized in engineering. Engineering systems can surpass biological systems in a number of cases with respect to individual characteristics.

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CONCLUSION

The time in which we are living is frequently referred to as the era of space flight, atomic energy, and cybernetics. The rapid development of science and technology with its characteristic overlapping of scientific disciplines and the continual emergence of new scientific trends has not bypassed medicine, i.e., one of the most ancient fields of the conscious and creative endeavor of man. Many people today speak of the backwardness of medicine with respect to the overall level of modern science. One of the ways of raising it to this level is the extensive introduction of technical means, primarily electronics and automation. The medical aspects of cybernetics are being considered at this time precisely with regard to this idea.

From our standpoint, both the reasons for the backwardness of medicine and the methods of raising it to the contemporary level are entirely different. The fact is that biological systems are incomparably more complex than the artificial, technical systems of modern science and technology. The simplified view of the living organism and the attempts at a mechanistic interpretation of a number of vital phenomena, or, conversely, vitalistic theories concerning the incognizance of a biological or psychic origin, have led to the fact that medicine is still using its thousand-year-old traditions to a greater extent than modern scientific and technical achievements. However, the main point now is not at all the technical outfitting of physicians and biologists with complex instruments and automatic devices. It is above all necessary to make a transition from empiricism to knowledge based on exact quantitative as well as qualitative, facts. The functional mechanisms of the elements of living systems should be studied and mathematical relationships between them should be found. An engineer is able to quite accurately calculate the lifting capacity of an aircraft and to estimate its performance under various flight conditions and different loads even before testing it in the air. When a physician gives a patient some medicine, he has only an approximate knowledge of the mechanism of the interaction of this medicine with the living organism and it is absolutely impossible for him to calculate the individual optimum dose or to estimate the effectiveness of a therapeutic measure. This is all due to the absence of exact knowledge necessary for the formation of appropriate quantitative laws. For example, it would be good to have a nomogram for calculating therapeutic doses of aspirin as a function of body temperature, age, arterial pressure, type of illness, and other factors. If there was a formula which connected the concentration of an anesthetic in the blood with the parameters of an electroencephalogram, pulse rate, and depth of inhibition, the task of designing an automatic anesthesia device would be only a technical problem. Therefore, the chief task in applying cybernetics in medicine is the creation of a foundation for the ultimate transition from empirical or qualitative methods and procedures to exact, quantitative laws.

It is clear that this problem is too great and complex to speak of its total solution today. We can now only point out distant approaches, certain trends, and individual stages of research in this area. In spite of the apparent naïveté of a large number of cybernetic concepts of the living organism and its systems, it is precisely this sort of approach which will make it possible to utilize the existing methods of exact sciences, mathematics in particular, for the quantitative analysis of biological laws. It sometimes appears that cybernetic concepts simplify the well-known classical ideas, but this is often a psychological effect. What is clear, is simple; what is complex, is unclear. Behind the simplicity of cybernetic concepts there stands a powerful mathematical apparatus which makes it possible to calculate millions of combinations of a large number of simultaneously changing parameters with the use of modern computer technology. It should be noted that many of the "simple" cybernetic models have not been "made to order" for contemporary mathematics and require the development of new mathematical theories and ideas. This is why mathematicians are being drawn more and more to biology today, since this discipline contains the food for the further progress of mathematical science.

The use of cybernetic concepts in medicine and biology is not in the least connected with the simplification of classical concepts or existing theoretical views. Cybernetics is the science of highly complex systems, i.e., systems with probabilistic-statistical organizations. Unfortunately, it is not possible to formulate quantitative laws by using theoretical concepts, no matter how tempting and likely they may be, if these concepts have been formulated on the basis of experiments in which only a qualitative and sometimes one-sided analysis of the data has been performed. The method of formulating "simple" cybernetic concepts is nothing more than the analysis of biological laws, which precedes the future synthesis of the structural and functional properties of the living organism.

Most biologists and physicians now understand that cybernetics is a necessary element of modern medical education. A knowledge of the fundamentals of cybernetics will promote the synthetic understanding of a biological object as a complex system united by certain common principles. The individual theoretical and applied medical disciplines provide the physician with knowledge in a definite, strictly outlined field, frequently out of touch with adjacent disciplines. Cybernetics orients the physician precisely with respect to the interrelationship between the various fields of medical knowledge. Cybernetics is uniting the anatomic-physiological, clinical, philosophical, and methodological aspects into one entity and in time, undoubtedly, it will become one of the important subjects in the medical schools and a professional aid to the scientific worker and the practicing physician. The present state of affairs is such that it is still too early to speak of the extensive introduction of cybernetics into medicine; all we can do now is to develop research and experimental design in every conceivable way in order to lay the groundwork for the daily utilization of cybernetic principles and methods in medical science and practice. A clear understanding of the complexity of the problems involved is of extreme importance for the development of this research. We should resolutely condemn the misuse of cybernetic terminology and concepts for explaining complex and unclear biological problems. This will require the dissemination of correct information to extensive groups of the medical profession on the possibilities of cybernetics and its prospectives. Close daily contact between engineers, mathematicians, and biologists is also extremely important. Significant advances related to the use of cybernetics and medicine can be made only with the combined efforts of scientific workers, physicians, engineers, and mathematicians.

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Born in 1903. Graduated from medical school in 1925. Awarded the rank of professor in 1933.

For forty years V. V. Parin has been performing extensive research in the field of circulatory physiology and pathology, the results of which have been acclaimed in the Soviet Union and abroad. Studies devoted to the application of advances made in cybernetics and electronics to the field of medicine occupy a significant place in Parin's research. During the last decade Parin and his associates have been working on problems of space biology and medicine. His research on the physiological functions of the organism under space flight conditions has become quite well known.

V. V. Parin has published over 150 scientific works, including several monographs.

ROMAN MARKOVICH BAYEVSKIY

Doctor of Medical Sciences. Born in 1928. Graduated from medical school in 1952. Has been involved with scientific work since his student days. One of Professor Parin's pupils. The majority of Bayevskiy's research has been associated with problems of cardiology, medical electronics, cybernetics, and space medicine. Bayevskiy has published more than 70 scientific works. He is well known as the inventor of an original ballistocardiographic sensor, which is described in his book, Osnovy prakticheskoy ballistokardiografii (Fundamentals of Practical Ballistocardiography). Bayevskiy is a well-known specialist on methods of physiological research in space and problems of automatic processing of medical information.

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